

# **Control and System Integration of Micro- and Nano-Scale Systems**

Report from the National Science Foundation workshop  
March 29–30, 2004

Edited by Benjamin Shapiro

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### ***Photo credits, front cover***

*(top to bottom)*

- 1) Micro Calorimeter. 1.8 mm plate, 3.5  $\mu\text{m}$  tether width. Chris Dubé, Draper Laboratory
- 2) Molecular dynamics simulation of water inside a functionalized carbon nanotube. N.R. Aluru, UIUC
- 3) Kinetic Monte Carlo simulation of gallium arsenide deposition. Martha Gallivan, Georgia Tech
- 4) A structure that grabs a masago (sushi) egg. Chang-Jin “CJ” Kim, UCLA
- 5) Metin Sitti, Nano Robotics Lab, Carnegie Mellon University
- 6) Lactoferrin Transition from 1lfg.pdb to 1lfh. Gregory Chirikjian, Robot and ProteinKinematics Lab, Johns Hopkins University

*Report graphic design and production: Rebecca Copeland, Institute for Systems Research, University of Maryland*

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# **Control and System Integration of Micro- and Nano-Scale Systems**

**Report from the National Science Foundation workshop, March 29–30, 2004**

*Edited by:*

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Dr. Gregory Chirikjian, Johns Hopkins University

Dr. Liwei Lin, University of California at Berkeley

Dr. Costas Maranas, Pennsylvania State University

Dr. Marvin White, Lehigh University

Dr. Minami Yoda, Georgia Institute of Technology

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## Table of Contents

Executive Summary.....	7
Workshop History and Format .....	7
System Integration: Needs in Measurement and Modeling for Control and Design .....	8
System Control: Applications in Fabrication, Object Manipulation, On-Chip Control, ..... and Control of Systems Combining Biology and Engineering	9
Education, Collaboration, and Infrastructure Recommendations.....	11
Summary .....	12
Appendix I: Workshop Program and Seminar Abstracts .....	13
Appendix II: Participant Quad Charts Organized by Theme Areas.....	19
<i>Biological (or Biomolecular/Biochemical) and Chemical Systems on Micro/Nano- Scales .....</i>	<i>19</i>
Paul Barton, MIT.....	20
Greg Chirikjian, Johns Hopkins University .....	21
Panagiotis Christofides, UCLA.....	22
Chris Dube, Charles Stark Draper Laboratory .....	23
Allison Ficht, Texas A&M University HSC .....	24
Costas Maranas, Penn State .....	25
Nitish Thakor, Johns Hopkins University.....	26
<i>BioMEMS and/or Nanobiotechnological Systems .....</i>	<i>27</i>
Michael Cima, MIT .....	28
Charles Eggleton, UMBC .....	29
Gennady Friedman, Drexel University .....	30
Joe Gatewood, SeiraD .....	31
Jongyoon Han, MIT .....	32
Michael Heller, University of California, San Diego .....	33
Noo Li Jeon, University of California, Irvine .....	34
Jack Judy, UCLA .....	35
John Koschwanetz, University of Washington .....	36
Per Reinhall, University of Washington .....	37
William Tang, University of California, Irvine .....	38
Joel Voldman, Massachusetts Institute of Technology .....	39
Yitshak Zohar, University of Arizona .....	40



---

***Control Systems with a MEMS and/or Nano Perspective ..... 41***

John Birdwell, The University of Tennessee .....	42
Jason Gorman, National Institute of Standards and Technology.....	43
Carl Knospe, University of Virginia .....	44
Mayuresh Kothare, Dept. of Chem. Eng., Lehigh University.....	45
Robert M'Closkey, UCLA .....	46
Kameshwar Poolla, UC Berkeley.....	47
Harshad Sane, Corning-IntelliSense.....	48
Benjamin Shapiro, University of Maryland .....	49
Marwan Simaan, University of Pittsburgh.....	50
Metin Sitti, Carnegie Mellon University .....	51
Mikhail Skliar, University of Utah.....	52
Tzyh-Jong Tarn, Washington University .....	53
Marc Weinberg, Draper Laboratory .....	54
Takis Zourntos, Texas A&M University .....	55

***Measurement, Modeling, and Model Validation at the Micro- and Nanoscale ..... 56***

Ali Beskok, Texas A&M University .....	57
Kenny Breuer, Brown University.....	58
Albert (Terry) Conlisk, Ohio State University .....	59
Martha Gallivan, Georgia Tech .....	60
Thomas Jones, University of Rochester.....	61
Andrew Ketsdever, Air Force Research Laboratory .....	62
Pramod Khargonekar, University of Florida .....	63
James Liburdy, Oregon State University.....	64
Ajay Malshe, University of Arkansas .....	65
Arvind Raman, Purdue University .....	66
Murti Salapaka, Iowa State University .....	67
David Stroud, Ohio State University .....	68
Jacob White, MIT .....	69
Minami Yoda, Georgia Institute of Technology .....	70

***MEMS Design/Fabrication, Devices, and Systems ..... 71***

Jordan Berg, Texas Tech University .....	72
Bishnu Gogoi, Motorola Sensor Products Division .....	73
David Horsley, University of California, Davis.....	74

Amit Lal, Cornell University .....	75
Y. C. Lee, University of Colorado .....	76
Woo Lee, Stevens Institute of Technology .....	77
Qiao Lin, Carnegie Mellon University .....	78
Mike Ramsey, Oak Ridge National Laboratory.....	79
Florian Solzbacher, University of Utah .....	80
Darrin Young, Case Western Reserve University.....	81
Babak Ziaie, University of Minnesota.....	82
<b>Nanoscale Fabrication .....</b>	<b>83</b>
George Barbastathis, Massachusetts Institute of Technology.....	84
Tianhong Cui, University of Minnesota-Twin Cities.....	85
Jun Jiao, Portland State University .....	86
Nikolai Lebedev, US Naval Research Lab .....	87
Liwei Lin, UC-Berkeley .....	88
Efstathios Meletis, Louisiana State University.....	89
Brad Paden, UC Santa Barbara.....	90
Massood Tabib-Azar, Case Western Reserve University .....	91
Fred Terry, University of Michigan .....	92
<b>Miscellaneous.....</b>	<b>93</b>
Narayan Aluru, University of Illinois at Urbana-Champaign .....	94
Rod Beresford, Brown University .....	95
Daniel Burns, Air Force Research Laboratory.....	96
Cetin Cetinkaya, Clarkson University.....	97
Tim Dallas, Texas Tech University.....	98
Gary Fedder, Carnegie Mellon University .....	99
Albert Henning, Redwood Microsystems, Inc.....	100
Peter Hesketh, Georgia Institute of Technology .....	101
Roberto Horowitz, UC Berkeley .....	102
Chang-Soo Kim, University of Missouri-Rolla .....	103
Martin Schmidt, MIT .....	104
Sharon Smith, Lockheed Martin Corporation .....	105
Shankar Sundaram, CFD Research Corporation .....	106
Marvin White, Lehigh University .....	107

## Executive Summary

This report summarizes the findings and recommendations of ninety experts in control, modeling, system integration and micro/nano-scale fabrication who met at the National Science Foundation for a two-day workshop in March 2004. The goal of the workshop was to identify research and education issues that must be addressed to enable the transition from micro and nano components to integrated systems. Discussions were organized around six theme areas, and only those research directions that required multi-disciplinary collaboration between themes are listed here. Recommendations are grouped according to three subjects: system integration, system control, and education and infrastructure needs.

System integration refers to combining numerous micro/nano components to form integrated systems, such as implantable drug delivery systems, micro machines (for instance, artificial insects or miniaturized surgical robots), and bio-chemical pathogen detection systems. Participants recommended research in two topics that could not be addressed by fabrication researchers alone, namely: the development of diagnostics and characterization tools for micro- and nano-scale systems; and the creation of parsimonious (keep essentials only) mathematical models that will enable system design, optimization, and control.

System control recommendations were focused on: control of fabrication processes to improve the manufacture of micro/nano systems (off-chip control), and on incorporating control into micro/nano systems to enable new and improved functionality (on-chip control). Topics included: research in fabrication process control; control for nano assembly and manipulation; requirements for the development of 'on-chip' control to direct the internal behavior of micro- and nano-scale systems; comments on the challenges in controlling heterogeneous systems; and research needs relevant to control of systems that combine biology and engineering.

The education and infrastructure recommendations were focused on training the next generation of cross-disciplinary students and faculty, and on modeling, measurement, and fabrication infrastructure needs.

## Workshop History and Format

The workshop organizing committee, consisting of Benjamin Shapiro (chair), Gregory Chirikjian, Liwei Lin, Costas Maranas, Marvin White, and Minami Yoda, was selected in December 2003, based on input from Maria Burka, Kishan Baheti, and Masayoshi Tomizuka at NSF. The committee formally announced the workshop in January 2004 and solicited applications from academia, industry, and government, until the closing date of March 1, 2004. Over four hundred applications were received. During the first week of March, the committee selected and invited ninety participants to attend the workshop.

Discussions at the two-day workshop were organized according to six theme areas:

1. Biological (or Biomolecular or Biochemical) and Chemical Systems on the Micro- and Nano-Length Scales
2. BioMEMS and/or Nanobiotechnological Systems
3. Control Systems with a MEMS and/or Nano Perspective
4. Measurement, Modeling, and Model Validation at the Micro- and Nanoscale
5. Micro-Electro-Mechanical-Systems Design/ Fabrication, Devices, and Systems
6. Nano Fabrication

On the first day of the workshop, the participants met within their respective theme areas. On the second day, the audience was randomized across themes so that researchers in nano fabrication, for example, would interact with researchers in controls. Each theme area was charged with producing a short list of cross-disciplinary recommendations (each recommendation would require a collaborative effort between at least two themes) that would address micro/nano system integration and control challenges.

This report is a summary of the discussions and recommendations at the workshop. An electronic copy of this report and further details, such as the workshop program and participant quad charts, are available at: [www.isr.umd.edu/CMN-NSFwkshp/](http://www.isr.umd.edu/CMN-NSFwkshp/).

## **System Integration: Needs in Measurement and Modeling for Control and Design**

System integration goals included: integration across length and time scales (from nano meters and femto seconds up to meters and years); integration between soft and hard fabrication techniques; integration of inorganic, organic, and living biological materials; and integration of in-situ sensors, actuators, and components for real time systems control. The benefits of feedback control that have been demonstrated on the macro scale (such as the ability to guarantee robust high performance in uncertain noisy environments, even in the presence of sub-system failures) are also required on the micro- and nano-scale. Participants identified research in measurement techniques and the development of parsimonious (essentials only) models as two major needs. Research in these two areas will improve the physical understanding needed for system integration and enable the models and real time sensing capabilities required for feedback control. It was also noted that industry should become involved as early as possible in the modeling and simulation process so that practical issues, such as common system failure modes and the effect of harsh environments, can be incorporated into the modeling effort.

### ***Systems Level Measurement: Diagnostics and Micro/Nano-Sensors***

To enable system integration workshop participants recommended research investment in diagnostics and sensors from the component to the systems level. Improved diagnostics (detailed and comprehensive measurement techniques) are required to: i) clarify physical phenomena that are dominant at the micro- and nano-scale; ii) provide basic input to physically based models – a lot of basic fluid/solid properties are still largely

unknown; and iii) validate both physically-based and reduced-order models. Whereas diagnostic techniques refer to laboratory measuring systems, sensors refer to devices that can be incorporated into a micro/nano-system and provide less detailed or single point measurements. Integration of sensors (and actuators) into a micro/nano-scale system remains a major fabrication and system integration challenge whose solution is required to enable real-time control: both in terms of allowing control of behavior inside micro- and nano-scale systems and in terms of using micro/nano-scale sensors and actuators for sensing and control of behavior externally on a larger scale. Challenges include: incorporation of sensors within a very limited space, sensor accessibility (getting signals in and out), and limiting the addition of any sensor fabrication steps that may reduce system yield.

### ***Parsimonious (Keep Essentials Only) Models for System Design and Control***

Both system optimization and control design typically requires models of the system, actuators, and sensors. Models used should be carefully chosen: they must contain enough physics to be predictive, but they must remain computationally tractable to enable design and control. At present, there is a disconnect between available micro/nano modeling tools and analysis, design, and control needs. For example, finite element models are commonly used to represent MEMS systems but these models cannot be used directly for control design and control implementation. Research should focus on creating minimal models for classes of micro- and nano-scale systems. Minimal models can be accomplished by combining physical insight (what are the dominant physics?) and model reduction techniques (dramatically reduce model size with a minimal sacrifice of model accuracy). Methods are needed to determine the point at which a model is good enough, and to validate such models using a combination of (more computationally expensive) physical first principle models and a reasonable number of (difficult, expensive, and time-consuming) experiments.

It was also recognized that there is a need to bridge the gap between molecular scale modeling and continuum length and time scales. For example, molecular dynamic simulations, though providing a tool for predicting behavior at the atomic scale, cannot reach the length and time scales of interest for system design. There is a need to create/extend averaging or model reduction tools that can provide the link between molecular and continuum scale models.

## **System Control: Applications in Fabrication, Object Manipulation, On-Chip Control, and Control of Systems Combining Biology and Engineering**

Feedback control is ubiquitous in engineering and biological systems: both engineering and living systems use feedback loops to sense and correct for departures away from desired performance. These sense-compare-and-react loops allow integrated systems to function reliably and with high performance even in the presence of noisy environments, unknown parameters, changing requirements, and sub-system failures. Workshop participants saw many opportunities for feedback control to contribute to micro- and nano-scale systems development. There were examples where micro-systems combined with control algorithms could be used to create and manipulate nano objects; feedback control could be used to handle uncertainty and limit the variability of nano-fabrication techniques; and, using nano-scale systems, there are opportunities to understand, access, and adapt molecular based “wet-ware” control loops inside biological systems. It was recommended that expertise in MEMS fabrication be used to create microscale testbeds for fabrication, handling, analysis, and control of nanoscale systems.

### ***Fabrication Process Control***

It was noted that it is difficult to achieve reproducible fabrication results at the nano-scale: for example, when fabricating carbon nano-tubes, “we repeat the same procedure and get different results each time,” Jun Jiao (Portland State).

Clearly, there is a lack of knowledge off and an inability to prescribe the relevant process parameters. Control was seen as an enabling technology that, through real-time process monitoring and appropriate actuator responses, would be able to help identify and control process parameters, and thereby improve device yield and reproducibility. Further, yield and fabrication reproducibility should be considered as research issues on the same level as the development of new fabrication processes. To enable process control, sensor and actuator type and placement issues should be considered at the early stages of the fabrication plant design: if these issues are only addressed after the plant has been built, it may be impossible to include the type of sensors and actuators needed for real-time process control. Efforts should focus on isolating the dominant physical phenomena in nano growth and deposition, important process control parameters must be identified and their effects must be understood, real time sensors must be developed and integrated into the fabrication plants, and effective control algorithms must be developed and validated.

There is also an intriguing possibility to use micro-systems and control to generate nanosized features, in short: “micro + control = nano.” Liwei Lin (Berkeley) showed a case where resistive heating (control) applied to a microbridge created nanowires. Hence an opportunity exists to exploit interesting physics (growth instabilities, parameter dependent self-assembly) to create and shape nano-objects using control theory and MEMS platforms.

### ***Control for Nano Assembly and Object Manipulation***

Atomic Force Microscopy (AFM) probes can be used to push, pull, cut, indent, and lithographically deposit nanoscale objects. Open control challenges for nanorobotic manipulation are summarized in the report from the 2003 “NSF workshop on Future Directions in Nano-Scale Systems, Dynamics and Control,” Metin Sitti (CMU) available online at [www.me.cmu.edu/faculty1/sitti/NSF\\_Report\\_Sitti.PDF](http://www.me.cmu.edu/faculty1/sitti/NSF_Report_Sitti.PDF). They include: generation of autonomous AFM systems for imaging and 3-dimensional, parallel manipulation;

in-situ real-time nano-scale control concepts for high-frequency nano-electromechanical systems; and hybrid modeling (continuous and discrete, multi length and time scales) of nano-mechanics to enable control design and implementation.

### ***'On-Chip' Control Inside Micro/Nano Systems***

For self-contained miniaturized systems, the sensors, actuators, and control hardware must be included inside the system. On-chip 'control inside' packaging is required for miniature systems such as implantable drug delivery platforms, micro sense-and-report systems, and, in the long term, micro-robots such as artificial insects. Integrating the control into the micro- or nano-scale system raised additional issues: i) Sensors, actuators, and control logic circuits must be optimally distributed inside a very small volume; ii) In many instances software and DSP based control is not practical (it takes up too much real estate and cannot address the fast dynamics found on the nanoscale) and analog type controllers must be designed instead; and iii) There is a need for a high degree of robustness and fault tolerance especially when the miniaturized system must operate inside unknown, hostile environments which can cause a large number of the sensors and actuators to fail. It was felt that robust control, distributed control, model reduction, state estimation, and optimization tools could be used to effectively address these questions.

### ***Control of Heterogeneous Systems***

On the micro- and nano-scale, there are interactions between continuous and discrete dynamics: micro-fluidic devices often have continuum flows but contain discrete objects such as cells or DNA chains that display stochastic motion; there is coupling between disparate length and time scales: phenomena on the macro scale can be used to control behavior on the nano scale and vice versa; and there is cross talk between interfacial and bulk phenomena. For systems that include organic or biological materials, the interfaces between inorganic and organic/biological components are heterogeneous and they must also be understood and controlled.

Thus, there is a need to develop modeling and control tools to address heterogeneous systems. This is a challenging area that is already receiving attention within the controls community. It was judged that, although there are notable exceptions, there is currently an insufficient link between efforts underway in the controls community and research carried out by scientists in micro/nano fabrication, chemistry, biology and modeling. It is recommended that collaborative teams of researchers (including control and micro/nano experts) focus on developing tools for specific sub-areas, such as control of discrete objects inside continuum flows or control of chemical processes at interfaces.

### ***Control of Systems that Combine Biology and Engineering***

BioMEMS and control workshop participants noted the tremendous opportunity for implantable medical sensors and systems. Applications raised at the workshop included miniaturized hearing aid implants, neural prostheses, in-vivo active blood pressure controllers, and glucose monitoring and drug delivery systems for diabetes management. Research is required to better address problems of coupling the sensor (materials, contact geometry, sensing modality, etc.) with the biology sample (cells, blood, tissues, etc.). It is necessary to address issues related to physical and chemical adaptation and to better control device surfaces to conform to cell growth. There is a need to improve the measurement and data extraction methods by which the true responses from the targeted entities (DNA, proteins, drugs, metabolites, etc.) is detected and transduced more sensitively and selectively from the large amount of non-specific and background interferences. The control algorithms that will control the behavior of the implantable devices must be developed. These algorithms must adapt to biological conditions and must work together with the complex feedback mechanisms found in the human body.

Conversely, using micro- and nano-scale measurement techniques there is now a real opportunity to learn from biological systems that are truly amazing examples of complex, integrated, micro/nano systems with feedback control. Ideas

for study of biology based control approaches include: i) In organisms, random processes generate organized structures at larger scales. Based on this, it should be possible to learn to control random, distributed, (self organizing) processes to create and direct desired structures. ii) Natural biomolecular processes are often based on nano-structure “interlocking” molecules that control the self-assembly of complex structures. There is a possibility to use fabricated structures, polymers, and genetically engineered microorganisms (for example, as used by Angela Belcher, MIT) to control the assembly of micro/nano systems. iii) Nature routinely implements wet-ware (chemically based) sensing, feedback, control, and automation in biological systems. There is a potential to mimic this capability and to engineer molecular pathway (chemical and biochemical) based sensing, actuation, control, networks, logic, and system architectures to perform desired tasks.

## Education, Collaboration, and Infrastructure Recommendations

A repeated topic across all themes in the workshop was the need to educate the next generation of students, and faculty, in a cross-disciplinary fashion, cutting across traditional lines of math, physics, biology, and mechanical, electrical, and chemical engineering. As in many other areas, there is an inability to communicate effectively across disciplines: this makes it especially difficult to effectively describe and design systems that combine different specializations. A variety of mechanisms were suggested to address this need, many of which are already being implemented: i) Funded cross-disciplinary student exchange programs should be established/expanded whereby students in discipline A can spend a summer or a year doing research in discipline B; ii) Students should be co-advised by professors in different fields, and, importantly, funding mechanisms should be established which will encourage such co-advising; iii) More programs are needed for cross-disciplinary education of working engineers and training courses for technicians in state-of-the-art fabrication techniques; iv) Support should be provided for summer workshops in specific topics such as AFM, microfluidics, nanofabrication, and bio-systems – it was suggested that

workshops follow the Gordon conferences model of a small number of scientists in a relaxed setting with a large amount of time set aside for informal discussions; v) Cross-disciplinary curricula should be developed at both the undergraduate and graduate level; and vi) There should be mentoring of junior faculty by senior faculty in other fields and funding mechanisms to permit and encourage faculty to take sabbaticals in areas outside their main expertise. A key concern was the nature of the tenure process: faculty should be encouraged, not penalized, to collaborate and write joint papers with scientists in other disciplines.

Insufficient infrastructure and mismatch of tools was a pervasive theme. Commercial modeling tools such as Coventor and Fluent have begun addressing phenomena on the micro- and nano-scale but, due to their computational complexity and the lack of accessibility to internal equations and algorithms, the resulting tools are not yet appropriate for control design and system integration. Some software companies are making an effort to address this need: CFDRC has a research effort in creating optimization ready models and FEMLAB software permits the creation of open source, coupled, PDEs (Partial Differential Equations) models. To help satisfy this need of design and control ready models, a peer reviewed database of software tools and public domain models for various sub-classes of micro- and nano-scale systems should be created: such a database must consolidate input from model developers *and* model users.

Similarly, access to standardized micro-fabrication techniques, especially for bio-chemistry, bio-medical, and related researchers should be improved. The availability of present foundry resources, such as MOSIS, MEMS Exchange, MUMPs, and Sandia’s SUMMiT, for MEMS and microelectronics, is acknowledged. However, aside from devices (not processes) offered through the Center for Neural Communication Technology at the University of Michigan, few resources exist which extend present foundry resources to the spheres of bio-chemistry and bio-medical engineering. And no resources extend the foundry concept to the nano-scale in general. To address the fabrication need it was recom-

mended that facilities be developed to extend the foundry concept to the nano-scale, and to the spheres of bio-chemical and bio-medical engineering.

Finally, there is a lack of diagnostics tools to characterize effectively both micro- and nano-scale systems. Although diagnostics tools exist for electrical phenomena, diagnostics for chemical, biological, thermal, optical, fluidic, and mechanical processes are much less well advanced. To address the measurement need, resources must be devoted to develop and make available micro/nano diagnostics tools.

## Summary

This document lists recommendations on combining the techniques of systems and control with research in micro- and nano-scale fabrication. The match between these two areas is timely and is of benefit to both groups. Micro- and nano-scale fabrication techniques are moving from components and devices to complex systems – researchers in this area can benefit from controls and system integration tools that address component coupling, the management of and design for uncertainty, and system optimization and control. Controls researchers are now developing powerful tools in distributed control – they can benefit from the distributed actuation and sensing opportunities that are afforded by numerous tiny sensors and actuators packed into small volumes or scattered across large ones. Moreover, by using micro- and nano-scale measurement techniques, scientists now have access to the inner molecular workings of biological systems: there is no doubt that control researchers can learn a tremendous amount from the phenomenal control systems found inside living organisms.



## Appendix I: Workshop Program and Seminar Abstracts

### *National Science Foundation workshop on Control and System Integration of Micro- and Nano-Scale Systems*

#### **Monday March 29**

##### **Morning**

7:00–7:30	Front Desk	(all laptops checked for viruses at NSF, go to room 357)
7:30–8:00	Room 375	Breakfast
8:00–8:30	Room 375	<b>Welcome and introduction to the workshop</b> Benjamin Shapiro; University of Maryland Maria Burka, Delcie Durham, Masayoshi Tomizuka, Kishan Baheti; NSF
8:30–9:10	Room 375	<b>Wireless Integrated MicroSystems (WIMS): Coming Revolution in the Gathering of Information</b> Ken Wise, University of Michigan
	Room 375	<b>Introduction to the six theme areas:</b>
9:20–9:40		<i>MEMS Design/Fabrication, Devices, and Systems: Research Directions in MEMS</i> Martin Schmidt, MIT
9:40–10:00		<i>Nano Fabrication: A Review of Nanofabrication Efforts and Challenges</i> Jun Jiao, Portland State University
10:00–10:15		Break
10:15–10:35		<i>BioMEMS and/or Nanobiotechnological Systems: MEMS for Biomedical Applications</i> Bill Tang, Irvine
10:35–10:55		<i>Biological (or Biomolecular or Biochemical) and Chemical Systems on the Micro- and Nano-Length Scales: Challenges and Opportunities in Biological Systems Analysis and Design</i> Costas Maranas, Penn State
10:55–11:15		<i>Control Systems with a MEMS and/or Nano Perspective: Dynamics and Control of Thin Film Microstructures</i> Panagiotis Christofides, UCLA
11:15–11:35		<i>Measurement, Modeling, and Model Validation at the Micro/Nanoscale: Modeling Transport in Micro and Nanofluidic Devices</i> Terry Conlisk, Ohio State University
11:40–Noon	Room 375	<b>Charge to breakout groups</b> Benjamin Shapiro, UMD Pickup lunch provided in/outside room 375. To be taken by workshop participants to breakout rooms.

##### **Afternoon**

Noon–2:30	<b>Theme breakout sessions (working lunch)</b> Participants go to the room that corresponds to their primary theme: the theme that they applied under. (People who applied under the theme “other” are free agents: they will go to theme that they feel most closely matches their expertise.)	
Noon–2:30	Room 330: <b>MEMS</b>	Panel: Berg, Lal, Solzbacher
Noon–2:30	Room 375: <b>Nano</b>	Panel: Meletis, Terry, Tabib-Azar, Cui
Noon–2:30	Room 530: <b>Bio-MEMS</b>	Panel: Eggleton, Heller, Friedman
Noon–2:30	Room 130: <b>Bio-Chem Systems</b>	Panel: Dube, Barton
Noon–2:30	Room 580: <b>Control</b>	Panel: Knospe, Zourntos, Devasia, Simaan
Noon–2:30	Room 680: <b>Measurement/Modeling</b>	Panel: Beskok, Salapaka, Liburdy, Gallivan
2:30–3:00	Break	(Theme representatives prepare their charts.)

3:00–3:45	Room 375	<b>Micro and Nano-Scale Systems for the Acquisition of Chemical and Biochemical Information</b> Mike Ramsey, Oak Ridge National Lab
	Room 375	<b>Theme representatives report back to main audience</b>
3:45–4:00	<b>MEMS</b>	(presented by theme representative)
4:00–4:15	<b>Nano</b>	(presented by theme representative)
4:15–4:30	<b>Bio-MEMS</b>	(presented by theme representative)
4:30–4:45	<b>Bio-Chem Systems</b>	(presented by theme representative)
4:45–5:00	<b>Control</b>	(presented by theme representative)
5:00–5:15	<b>Meas/Modeling</b>	(presented by theme representative)
5:15–6:30	Room 375	<b>Discussion in main audience</b>
6:30	<b>DINNER</b> —a list of restaurants in the area will be provided. Further ad hoc discussions during dinner.	

## **Tuesday March 30**

### **Morning**

7:30–8:00	Room 375	Breakfast
8:00–8:40	Room 375	<b>Design and Engineering of Bio-Molecular Nano-Devices and Systems</b> Anantha Krishnan, DARPA
8:40–9:00	Room 375	<b>Workshop report from NSF Nanoscale Systems, Dynamics and Control, ACC 2003</b> Metin Sitti, CMU
9:05–11:30	<b>Theme breakout sessions with re-organized audience</b> Participants organized by secondary (randomly chosen) theme, see participants list. Continue discussions and incorporate comments from previous day, formulation and prioritization of research directions, etc.	
9:05–11:30:	Room 365: <b>MEMS</b>	Panel: Berg, Lal, Solzbacher
9:05–11:30:	Room 375: <b>Nano</b>	Panel: Meletis, Terry, Tabib-Azar, Cui
9:05–11:30:	Room 530: <b>Bio-MEMS</b>	Panel: Eggleton, Heller, Friedman
9:05–11:30:	Room 380: <b>Bio-Chem Systems</b>	Panel: Dube, Barton
9:05–11:30:	Room 580: <b>Control</b>	Panel: Knospe, Zourntos, Devasia, Simaan
9:05–11:30:	Room 730: <b>Measurement/Modeling</b>	Panel: Beskok, Salapaka, Liburdy, Gallivan
11:30–Noon	Break	(Theme representatives prepare their charts.)
	Room 375	Theme representatives report back to main audience.

### **Afternoon**

Noon–12:10	<b>MEMS</b>	(results presented by theme representative)
12:10–12:20	<b>Nano</b>	(results presented by theme representative)
12:20–12:30	<b>Bio-MEMS</b>	(results presented by theme representative)
12:30–12:40	<b>Bio-Chem Systems</b>	(results presented by theme representative)
12:40–12:50	<b>Control</b>	(results presented by theme representative)
12:50–1pm	<b>Meas/Modeling</b>	(results presented by theme representative)
1pm–2pm	Room 375	<b>Discussion in main audience</b> (Lunch is provided.) <b>Workshop summation</b>
2:00pm	Adjourn	

## Seminar Abstracts

### Wireless Integrated MicroSystems (WIMS) Coming Revolution in the Gathering of Information

*Ken D. Wise*

*Engineering Research Center for Wireless Integrated  
MicroSystems  
The University of Michigan*

Wireless integrated microsystems promise to become pervasive during the coming decade in applications ranging from health care and environmental monitoring to homeland security. Merging micropower embedded computing, wireless interfaces, and wafer-level packaging with microelectromechanical systems (MEMS), the resulting button-sized modules will serve as smart information-gathering nodes that will effectively wire the planet, extending communication networks to a wide range of new information-gathering applications. Target specifications for these microsystems include a size of <1cc, a power dissipation of <1mW, and a range from 1cm to 1km. Such devices will be built on generic platforms that are digitally compensated and self-testing, customized by software and by front-end sensor selection. This talk will discuss two emerging microsystems. A family of chronically-implantable neural prostheses integrates high-density three-dimensional microelectrode arrays with embedded signal processing and wireless telemetry, offering hope for the treatment of deafness, paralysis, epilepsy, and Parkinson's disease. These microsystems represent an electronic interface to the central nervous system at the cellular level. A wristwatch-size environmental monitor is also being developed to measure pressure, temperature, humidity, position, and air purity. Employing nanotechnology, the microsystem includes an integrated gas chromatograph capable of analyzing complex gaseous mixtures with sensitivities in the part-per-trillion range, offering exciting possibilities for enhancing homeland security and reducing global pollution.

## Research Directions in MEMS

*Martin A. Schmidt*

*Massachusetts Institute of Technology*

This talk begins with an overview on the current status of the MEMS field. Following this, we preview future directions. These future directions are cast in the context of area where MEMS technology plays an 'enabling' role: making it possible to do something not attainable at a larger scale. Examples in this domain include low-power wireless devices, microfluidic applications, and power MEMS. The manufacturing issues in this technology are also discussed.

### A Review of Nanofabrication Efforts and Challenges

*Jun Jiao*

*Physics Department, Portland State University*

In this talk, the most common methods used currently for synthesizing the building blocks for nanodevices and nanosystems were reviewed. The combination of "bottom-up", "top-down", and "self-assembly" was described as the main theme for developing integrated nano-scale systems. The example approaches provided by the participants of the workshop were demonstrated. The efforts summarized include (1) in-situ growth of carbon nanotubes and nanowires on designed specifications by chemical vapor deposition or by vapor-phase transport mechanism, (2) layer-by-layer putting down of nanoscale thin films, electrodes, and interconnectors, as well as other types of structural morphologies by means of electron beam lithography, soft lithography, and nano-imprinting, (3) creating inorganic/organic materials with nano-interface and functionality by self-assembling monolayers. It was also pointed out that to make nanoscale devices as reproducible and controllable as conventional silicon systems-on-chip requires seamless coordination and collaboration among partners from multiple disciplines. The challenge issues discussed include i) synthesis methodologies, ii) materials characterizations, iii) analytical tool development such as how to design the appropriate tools with the ability to directly image and characterize the

structures, defects, and interfaces in nanometer-scale and quantitatively measure their properties, and iv) computational modeling in particular in the area of developing computationally tractable strategies for modeling the assembly process of the nanoscale systems.

## **MEMS for Biomedical Applications**

*Bill Tang*

*University of California at Irvine*

The worldwide cost for healthcare, estimated at US\$2 trillion, is one of the strongest motivations to develop alternatives to the existing healthcare system. One of the alternatives is to decentralize healthcare by employing a broad range of enabling technologies. These technologies allow substantial cost reduction and miniaturization of conventional diagnostic equipment, prosthetic devices, and administration of therapeutics, as well as networked real-time monitors to enable at-home point-of-care. The use of MEMS and future advances in MEMS can strategically reach these goals. Current development of BioMEMS can be categorized into in-vivo and in-vitro uses, each of which is associated with a different set of requirements and design approaches. Common to both categories are the use of a broad range of materials other than silicon, hybrid integration, sensing and control at the molecular scale, and the continued exploration of new sensing mechanisms.

## **Challenges and Opportunities in Biological Systems Analysis and Design**

*Costas D. Maranas*

*Pennsylvania State University*

In this talk, we will discuss the application of systems engineering methodologies to address modeling and optimization challenges arising in protein and pathways engineering. In protein engineering, directed evolution methods are widely employed to combinatorially evolve proteins with improved properties for a wide range of applications. A computational framework using mean field energy calculations will be presented for identifying what patterns of recombination

events and/or mutations are likely to give rise to functional protein hybrids. In the second part of the talk, we will explore the use of bilevel optimization to suggest metabolic networks modifications that lead to targeted overproduction. We will also present a framework for efficiently analyzing the topological properties of genome-scale stoichiometric models revealing partial, total or even directional couplings between different reactions under a variety of conditions.

## **Dynamics and Control of Thin Film Microstructures**

*Panagiotis Christofides*

*University of California at Los Angeles*

We recently proposed a novel method for multivariable feedback control of surface roughness and growth rate in thin film growth using multiscale distributed models. To demonstrate our method, we used the process of thin film growth in a stagnation flow geometry and considered atom adsorption, desorption and surface migration as the three processes that shape film micro-structure and determine film growth rate. A multiscale model that involves coupled partial differential equations (PDEs) for the modeling of the gas phase and a kinetic MC simulator, based on a high-order lattice, for the modeling of film growth, was used to simulate the process. Using our method, a roughness and growth rate estimator was constructed that allows computing estimates of the surface roughness and growth rate at a time-scale comparable to the real-time evolution of the process. The estimator involves kinetic MC simulators based on small-lattice models, adaptive filters used to reduce stochastic fluctuations of the small-lattice MC simulator outputs and measurement error compensators used to reduce the error between the estimates and measurements. A multivariable feedback controller, which uses the state estimator and explicitly compensates for the effect of input/output interactions, was designed to simultaneously regulate the growth rate and surface roughness by manipulating substrate temperature and inlet precursor mole fraction. Application of the proposed control system to the multiscale process model demonstrated successful regulation of the surface rough-

ness and growth rate to the desired set-point values. The developed method was also used to control surface roughness and growth rate of GaAs (001) thin films produced by MOCVD using an experimentally-validated kinetic MC model.

### **Modeling Transport in Micro and Nanofluidic Devices**

*A. T. Conlisk*  
*Ohio State University*

In this presentation we outline the various methods modeling flow and transport of ionic and biomolecular species at the micro and nanoscale. It is well known that the volume flow rate varies linearly with channel height for electrically driven flow in contrast to pressure driven flow which varies as height cubed. This means that very large pressure drops are required to drive flows in small channels thus making electroosmotic flow the method of choice for flows in channels of the order of 1  $\mu\text{m}$  or less. In particular we review what can and cannot be done in the way of modeling and experimentation at the micro and nanoscale. For example, velocity, temperature and concentration profiles cannot be measured at nanoscale thus making the development of accurate models of complex transport phenomena even more important. Both liquid and gas flows are reviewed. Comparisons of our continuum modeling results with experimental data for channels as small as seven nanometers reveals that continuum models are very accurate in predicting global parameters such as flow rate even for small biomolecules such as albumin and glucose. Comparisons of continuum and molecular dynamics simulations at a channels height of three nanometers are also described.

### **Micro and Nano-Scale Systems for the Acquisition of Chemical and Biochemical Information**

*Mike Ramsey*  
*Oak Ridge National Laboratory*

Tremendous interest in microfabricated fluidic channel structures (microchips) has grown over the past decade due to the large number

of powerful demonstrations that have appeared in the literature. The diversity of chemical and biochemical measurement techniques implemented on microchips is large including various electrophoretic and chromatographic separations, chemical and enzymatic reactions, noncovalent recognition interactions, sample concentration enhancement, and cellular manipulations. In addition the types of samples addressed by microchips has been broad in scope, e.g., small ions and molecules, single and double stranded DNA, amino acids, peptides, and proteins. These devices have low cost and small footprints while consuming miniscule quantities of reagents and producing rapid results. Moreover, the manufacturing strategy used to make these devices, i.e., photolithography, allows highly parallel systems to be fabricated at low incremental cost. All of these features suggest the possibility to perform chemical experimentation at a massive scale at low cost on a bench top. More recently we have been investigating the prospects of shrinking channel lateral dimensions by a factor of 1000, i.e., to molecular length scales. A number of interesting capabilities are possible with nanoscale channels and pores including the structural characterization of single molecules. Fundamental studies of electrokinetic fluid transport in nanoconfined spaces have been investigated allowing the first experimental benchmarking of continuum theories for such phenomena that were developed decades ago. In addition, potential applications of devices with 100 nm features have been demonstrated. We are also investigating the possibilities of shrinking mass spectrometry to the palm-of-the-hand size. Examples will be presented showing various chemical and biochemical experiments that have been successfully transferred to these miniature platforms. Prospects for the future will also be discussed.

### **Design and Engineering of Nanoscale Bio-Molecular Devices and Systems**

*Anantha Krishnan*  
*Program Manager, Defense Sciences Office*  
*Defense Advanced Research Projects Agency*

Ongoing research in nanotechnology is starting to demonstrate controlled fabrication of high

quality nanostructures (nanoparticles, nanotubes, nanopores, etc.) that are capable of interacting with biology at the molecular scale. Significant recent accomplishments in biology and surface chemistry have also demonstrated programmed assembly of engineered molecular structures with excellent control on spatial distribution and orientation. Biological systems show remarkable sensitivity, specificity and efficiency due to the selective evolution of molecular mechanisms over millions of years. It is anticipated that the engineering of hybrid molecular assemblies involving bio-molecules would enable the exploitation of these unique aspects of biological systems while affording the control that is possible through nanotechnology. The development of novel biotic-abiotic interfaces will lead to 'smart' bio-molecular assemblies with new functionalities (e.g., nano-sensors, nano-power generators, nano-chemical factories, etc.) and significant advantages (over conventional engineering systems) in terms of size, power consumption, efficiency and ease of fabrication. This would also enable 'smart' large-scale integrated systems consisting of several such devices that demonstrate the attributes of automated adaptivity/reconfigurability, feedback control, fault tolerance and compensation at the system scale.

Current DARPA programs are focusing on methodologies for designing, fabricating and demonstrating different kinds of novel bio-molecular assemblies that form transducing elements between chemical, electrical, optical and mechanical phenomena. These would typically result in many functions at the molecular scale such as chemically induced nano-mechanical motion, optically/electrically induced chemical synthesis, chemically induced optical/electrical reporting mechanisms, etc. The ability to control and manipulate (i.e., address) these functions at the molecular scale as well as the ability to integrate several such devices to form larger scale systems are of primary interest. The programs are specifically targeting issues such as, (i) the identification of candidate bio-molecular devices and systems of interest, (ii) the determination of unique advantages (versus the current state-of-the-art) that these devices offer in terms of performance, cost, functionality, etc., (iii) the extraction of bio-

molecular devices from their natural environment without significant loss of performance, (iv) the engineering of these devices to realize new functionalities, and (v) the development of technologies to enable the large-scale integration of these bio-molecular nano-devices into systems.

Research in these areas is expected to lead to unique multi-disciplinary technologies that enable novel bio-molecular assemblies and a new generation of nano-devices/systems that will have a revolutionary impact on almost every discipline, especially health monitoring, wirelessly addressed implantable devices for drug delivery and cell/tissue repair, biological/chemical agents and explosives/mines detection, energy conversion, bio-catalysis, bio-engineered materials, molecular computing/information processing systems, etc.

### **Workshop Report from NSF Nano-Scale Systems, Dynamics and Control, ACC 2003**

*Metin Sitti  
Carnegie Mellon University*

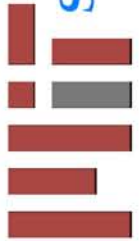
This presentation contains the findings of the first NSF workshop on the newly emerging area of nano-scale systems, dynamics and control. This workshop brought together many leading researchers from various disciplines and background for discussing the current status, future research directions, and potential applications of this new field. After giving a general background on nano-scale dynamics and systems, research problems and open issues related to Scanning Probe Microscopy dynamics and controls, nano-manipulation systems, directed self-assembly, nano-manufacturing, micro/nano-robotics, nano-electromechanical sensors and devices, micro/nano-electromechanical systems integrated with biological entities, and nano-scale human-machine interfacing are discussed. Next, current and future educational initiative possibilities are addressed. Finally, promising future directions and challenges are summarized.

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## Appendix II: Participant Quad Charts Organized by Theme Areas

### ***Biological (or Biomolecular/Biochemical) and Chemical Systems on Micro/Nano-Scales***

Paul Barton, MIT .....	20
Greg Chirikjian, Johns Hopkins University .....	21
Panagiotis Christofides, UCLA.....	22
Chris Dube, Charles Stark Draper Laboratory .....	23
Allison Ficht, Texas A&M University HSC .....	24
Costas Maranas, Penn State .....	25
Nitish Thakor, Johns Hopkins University.....	26



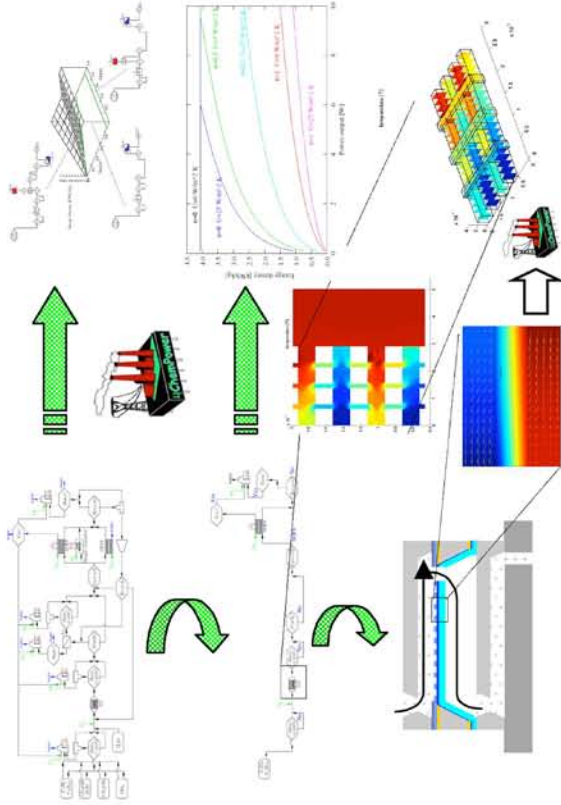
# Systems Engineering of Micro-Power Generation Processes

Paul I. Barton, Massachusetts Institute of Technology



## Goals and Potential Impact

- Replacement of batteries (low energy density, high cost and big environmental impact) with fuel cell systems (potential for very high energy density); large impact, since global battery market amounts to over \$35 billion
- Processes that are consumer products; different product specifications map to different optimal process structures; complex tradeoffs between design alternatives
- System wide modeling and integration tools for micro process systems and methodology for comparison of alternatives
- Design tools for integrated thermal management and plant layout
- Process operation without operators; design and formal verification of autonomous automation systems



## Approach and Accomplishments

- Equation-based steady-state and dynamic system wide modeling tools (ABACUSS, DAEPACK)
- Process-design based on highly interconnected devices rather than unit operations. Models with heat integration and heat losses
- Simulation studies of process superstructures embedding many process options; identification of promising process alternatives
- Computational fluid dynamics models of subset of alternatives
- Parametric mixed-integer optimization formulations for optimal process design as function of product specifications and unit performance parameters
- Global dynamic optimization algorithms for linear hybrid systems

## Open Research Questions

- Parametric optimization algorithms for general cases (e.g., parameter dependent technology matrix)
- Presentation to the decision maker of parametric optimization problem solutions in many dimensions
- Integration of system level models used for optimization with CFD models for detailed unit operation design
- Formal hybrid systems methods for design and verification of micro process automation systems



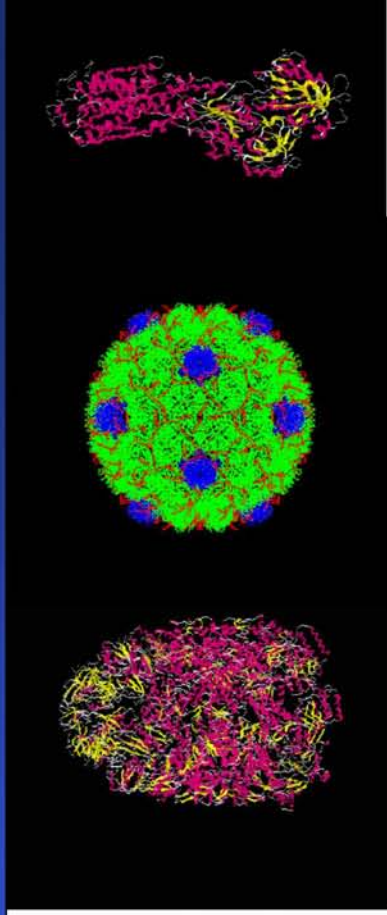
# Modeling Conformational Transitions in Macromolecules

Gregory Chirikjian  
Johns Hopkins Univ.

## Goals and Potential Impact if Successful

Model the kinematics and mechanics of biological macromolecules in order to:

- Understand better the mechanisms by which naturally occurring molecular machines function;
  - Establish design principles for man-made molecular machines
  - Develop plant models for such systems for use in control algorithms.
- Perform statistical (structural-bioinformatics) analysis of data in the protein data bank using theory of Lie groups and other mathematics developed in geometric control theory literature



Examples of Molecular Machines:  
(left) GroEL/GroES, HK97 Capsid,  
(right) Ion Channel

## Approach and/or Accomplishments

We have developed mechanical models of macromolecular motions and performed analyses such as those reported in:

- Lee, S., Chirikjian, G.S., ``Inter-Helical Angle and Distance Preferences in Globular Proteins," Biophysical Journal, Vol. 86, pp. 1105-1117, Feb 2004.
- Kim, M.K., Jernigan, R.L., Chirikjian, G.S., ``An elastic network model of HK97 capsid maturation," Journal of Structural Biology, 143 (2): 107-117 AUG 2003.
- Chirikjian, G.S., ``A Methodology for Determining Mechanical Properties of Macromolecules from Ensemble Motion Data," Trends in Analytical Chemistry, Vol. 22, No. 9, pp. 549-553, Sept. 2003.

## Bottlenecks and Open Research Questions

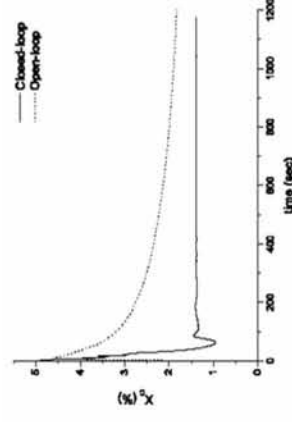
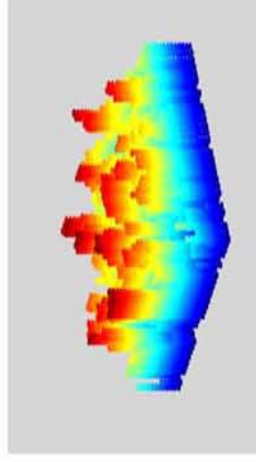
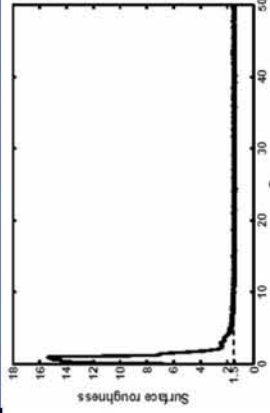
- Can we develop simplified models for extremely complex macromolecular systems, or must one use very detailed quantum-mechanical or all-atom classical chemical physics descriptions ?
- How do we bridge the gap between experimental and theoretical/computational research in this area ?
- Are there any natural boundaries between nanotechnology, structural biology, bioinformatics, and the computational modeling of biomolecular machines ?
- As with any cross-disciplinary effort, how do we establish appropriate metrics for evaluation of research quality?

# Feedback Control of Material Microstructure

Panagiotis D. Christofides  
University of California, Los Angeles

## Goals and Potential Impact if Successful

- Achievement of desired material microstructure and composition
- Implementation on detailed process models and experimental thin film growth processes.
- Development of novel feedback control methods by integrating multiscale distributed models and on-line measurement techniques
- Meet the increasingly stringent requirements on quality of semiconductor thin film from electronic chip industry.



## Approach and/or Accomplishments

- \*Multiscale Modeling:
  - Continuous PDE models for gas phase dynamics.
  - Stochastic models for thin film microstructure
- \*Real-Time Estimation:
  - Model reduction.
  - Correlation of real-time gas phase measurements to thin film composition and microstructure.
- \*Feedback Control Design:
  - Estimator/Controller structure.
  - Spatially distributed sensing and actuation.

## Bottlenecks and Open Research Questions

- \*Using stochastic multiscale models for controller design.
  - Methods for feedback controller design based on Monte-Carlo models.
  - Systematic model reduction techniques for stochastic PDE models.
  - Feedback controller design based on stochastic PDE models.
- \*Computational efficiency of simulators.
  - Possibility of implementation of Monte-Carlo simulation in multiple CPUs.



# Modeling and Control of Micro Calorimeter

Chris Dubé  
Draper Laboratory

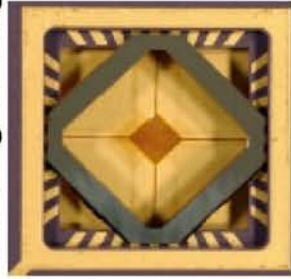
## Goals and Potential Impact

- Closed-loop differential calorimetry for:
  - High-throughput screening array
  - Gas-phase chemical sensing
- Calorimetry on microporous surface avoids long mixing time and provides well-less analysis
- High sensitivity sensing for:
  - protein-protein folding
  - DNA hybridization
  - small molecule-protein binding
- $10^{-8}$  J requires control-loop around dynamic system subject to thermal and electronic noise

## Technical Approach/Accomplishments

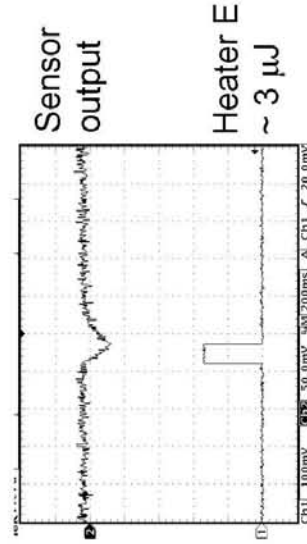
- (Mark Mescher, Amy Duwel, Keith Baldwin, Tom King)
- Modeling
    - Modeling of hybrid MEMS technology accurately predicts device performance w/o Rx.
    - Current best noise model predicts noise floor well below sensitivity objective ( $\sim 10^{-8}$  J).
  - Readout electronics calibrated using  $10^{-6}$  J pulse
  - PCB being designed to improve signal to noise ratio
  - Developing LabView data collection and processing

## Packaged single-element



1.8 mm plate  
35  $\mu$ m tether width

- Heating rates > 500  $^{\circ}\text{C/s}$
- Cooling time constants in air:
  - Empty plate: 0.11 s
  - With droplet = 2.4 s



## Open Issues and Research Questions

- Lack of models for calorimetry of biological system contained in microporous environment with uncertain hydration
- Surface regeneration for protein bound to sensor surface.
- Traditional understanding of macro scale solution-based calorimetry of biological systems not readily applicable to microscale reactions on surfaces
- Fidelity of Simulink model
  - Add noise sources
- Demonstration of  $10^{-8}$  J sensitivity

## Goals and Potential Impact if Successful

### Goals:

To implement, through emulsion and microfluidic technology, the use of novel proteins and peptides for 1) the production of micro and nanoscale release vehicles and 2) adhesives for an aqueous environment.

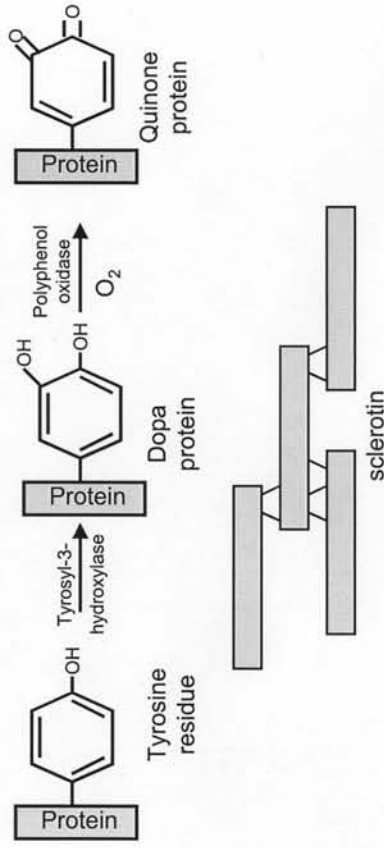
To use self-assembling proteins as scaffolds for controlled release vehicles.

Impact: Provide completely new and innovative solutions to controlled release at the micro and nanoscale level. Provide new adhesives for aqueous environments and self-healing applications for materials.

## Approach and/or Accomplishments

Using emulsion technologies, we have employed novel proteins and peptides for the production of controlled release systems. Taking advantage of quinone chemistry we have used protein derivatives as adhesives, mimicking natural processes and using the recombinant form of natural protein glue composites. Collaboration with engineers is opening new doors for assessment of materials properties and applications of these protein based glues and sealants.

## Chemical basis for glues and sealants



## Bottlenecks and Open Research Questions

How to interface biological and engineering systems at a practical level. To carry proof of concept into practice.

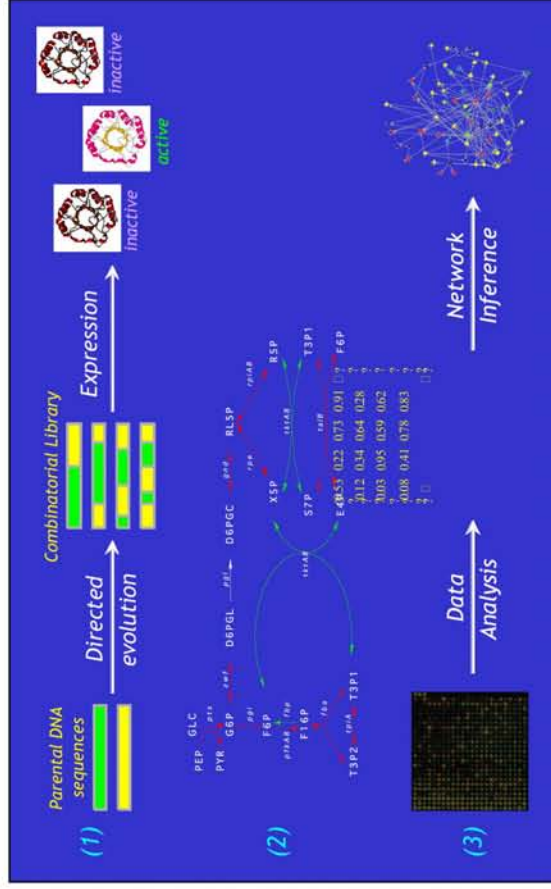


# Analysis and Design of Biological Systems and Networks

Costas D. Maranas  
Penn State

## Goals and Potential Impact if Successful

- Computational design of combinatorial protein libraries
- Design of “sensing” molecules
- Metabolic pathway analysis and optimization
- Topological analysis of structural features of biological networks
- Microbial strain optimization
- Elucidation and verification of regulatory networks
- Real options based planning approaches for R&D portfolio optimization



## Approach and/or Accomplishments

- Use of combinatorial optimization techniques (i.e., MILP and stochastic) to search through molecular and network alternatives.
  - Use of potential energy models of molecular interactions (i.e., CHARMM) and scoring functions to evaluate the strength of binding events.
  - Use of stoichiometry, regulatory informations and kinetic representations to describe interactions in metabolic and regulatory networks
- Moore, G.L. and C.D. Maranas (2004), "Computational Challenges in Combinatorial Library Design for Protein Engineering," *AIChE J.*, 50, 252-262.
- Saraf, M.C., A.R. Horswill, S.J. Benkovic, and C.D. Maranas (2004), "FamClash: A Method for Ranking the Activity of Engineered Enzymes," *Proc. Natl. Acad. Sci. USA*, in press
- Burgard, A.P., E.V. Nikolaev, C.H. Schilling, and C.D. Maranas (2004), "Flux Coupling Analysis of Genome-scale Metabolic Reconstructions," *Genome Research*, 14(2), 301-312
- Burgard, A.P., P. Pharkya, and C.D. Maranas (2003), "OptKnock: A Bilevel Programming Framework for Identifying Gene Knockout Strategies for Microbial Strain Optimization," *Biotechnology and Bioengineering*, 84, 647-657.

## Bottlenecks and Open Research Questions

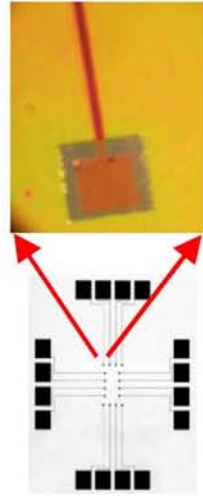
- How do we design customized molecular sensors with customized affinities for desired target molecules ?
- How can we elucidate the complex web of interactions in living systems ?
- How can we redesign living cells to be more attuned to engineering objectives such as overproduction or sensing?

## Goals and Potential Impact if Successful

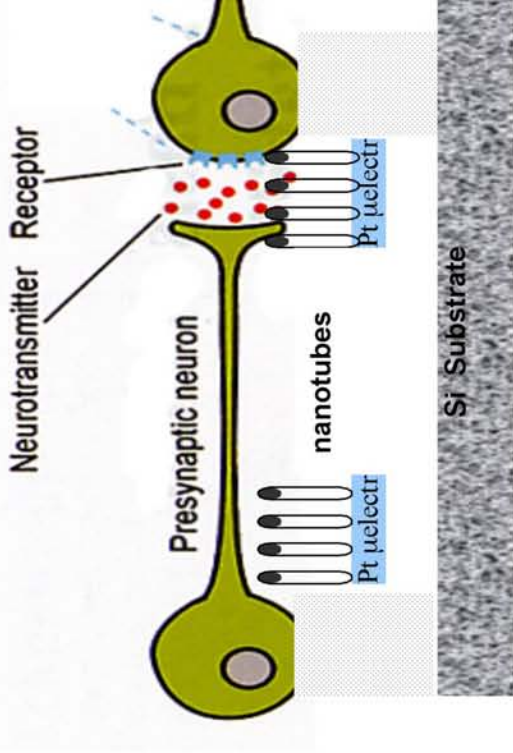
Our overall goal is to develop technology for neuroscience research. In particular, we are interested in sensing neurochemicals as single neuron and single synapse levels. Such unprecedented sensitivity would allow fundamental studies of distribution of neurochemicals in neural networks in culture, their measurement in *in vitro* models of stroke and epilepsy. In addition, we should be able to learn about synapse formation, synaptic plasticity and neural network formation.

## Approach and/or Accomplishments

We have developed a 1) neurochemical sensor using microfabrication processes, and 2) an integrated VLSI chip with pA or better sensitivity. Together these provided high sensitivity, multichannel measurement of neurochemicals such as dopamine and Nitric Oxide (NO).



Neurochemical sensor array and integrated VLSI interface.



## Bottlenecks and Open Research Questions

Our technological goal is to fabricate nanosensors on substrates compatible with neuronal cultures. The nanosensor fabrication must be temperature and process compatible. In addition, interfacing to nanowires to highly multiplexed VLSI circuit interface is a challenge.

Further, we would like to be able to couple various genetic material to the nanowires so that they can be delivered to the neurons at the site of synapse formation. Hence, nanowire/genetic material processes need to be developed that are mutually compatible.

### ***BioMEMS and/or Nanobiotechnological Systems***

Charles Eggleton, UMBC .....	28
Gennady Friedman, Drexel University .....	29
Joe Gatewood, SeiraD .....	30
Jongyoon Han, MIT .....	31
Michael Heller, University of California, San Diego .....	32
Noo Li Jeon, University of California, Irvine .....	33
Jack Judy, UCLA .....	34
John Koschwanez, University of Washington .....	35
Per Reinhall, University of Washington .....	36
William Tang, University of California, Irvine .....	37
Joel Voldman, Massachusetts Institute of Technology .....	38
Yitshak Zohar, University of Arizona .....	39
Michael Cima, MIT .....	40



# MEMS Devices for Controlled Release Drug Delivery

Michael J. Cima  
MIT

## Goals and Potential Impact if Successful

An implantable, micron scale drug delivery system for controlled release of chemical substances.

- Drugs in any format (solid, liquid, gel) can be delivered.
  - Most stable / efficacious format may be used
- Miniature chips allow local delivery
  - Reduced systemic toxicity for treatment of solid tumors
  - Circumvents blood brain barrier in brain tumor therapy
- Complex release profiles of multiple chemical substances
  - Any temporal release profile with time scale longer than individual release event.
  - "Pharmacy on a Chip"
- Can mimic body's natural production of chemical agents
  - ⇒ Potential "pacemaker" for the endocrine system

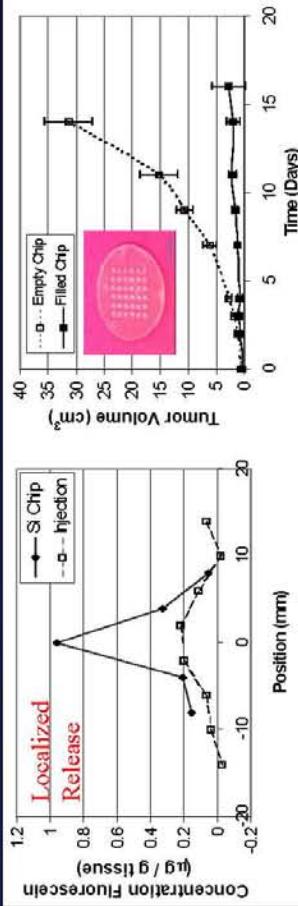
## Approach and/or Accomplishments

### Active Silicon-based MEMS Device

- Device fabricated by existing silicon micromachining techniques
- Substances released from reservoirs by electrochemical corrosion of membranes
- Control of spatial and temporal release profile, *in situ* monitoring of drug release demonstrated *in vitro* and *in vivo*

### Passive, Resorbable Polymer Device

- Polymer powder pressed into disc, membranes injected
- Composition, molecular weight of membranes adjusted to control temporal release profile
- *In vitro* and *in vivo* control of temporal release profile successfully demonstrated
- Delivery of BCNU effectively retards growth of 9L Glioma in rat flank



## In Vivo Release Results

- Active Si Device (Left)
  - Spatial localization (top)
  - Pulsatile release (bottom)
- Passive Polymer Device (Above)
  - Effect of BCNU delivery on growth of 9L glioma in rat flank

## Bottlenecks and Open Research Questions

### Device Reliability

- Hermetic seal must be achieved to prevent premature leakage of drug and possible loss of drug activity.
- Filling and payload formulation are important to achieving complete and timely delivery of the active substance
- Reliability of membrane activation must be ensured

### Long Term In Vivo Operation

- Influence of local inflammatory response on device operation is not currently well understood.

### Injectable Passive Device Format

- Best method for fabricating, filling, sealing syringe-injectable polymer device?



# A Cellular mechanics framework for MEMS/nano design and control

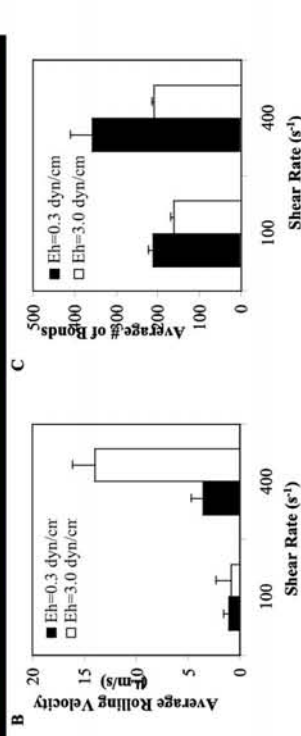
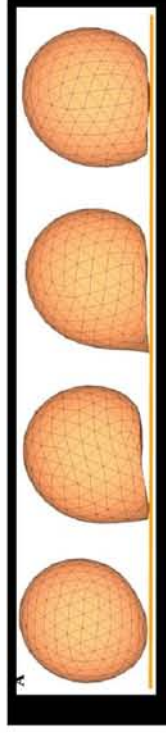
C. D. Eggleton  
UMBC

## Goals and Potential Impact if Successful

- **GOAL:** Develop models at the interface of fluid physics, vascular biology and nano-scale molecular interactions, and provide generalized computational tools that can be used to design, test and optimize strategies involving molecular interactions and bio-inspired particles.
- **IMPACT:** Predict mesoscale response of the composite system based on the properties of nanoscale constituents
- **IMPACT:** Model indicates optimum properties of nanoscale constituents from system viewpoint

## Approach and/or Accomplishments

- Immersed Boundary method coupled with Monte-Carlo simulation of cell-substrate molecular interactions shows deformable particles roll more slowly along surface in agreement with in vitro observations
- simulations yield number of molecular bonds and force exerted on each bond at every time step – currently not measured in vitro
- Boundary Integral Simulations indicate that increasing stiffness of cellular cytoskeleton (support scaffold) can lead to increased deformation-membrane rupture



**Simulation of leukocyte rolling on P-selectin coated surface under shear flow.** (A) Cell Profile. Variation in average rolling velocity (B), and average number of receptor-ligand bonds (C), with cell membrane stiffness at low and high shear rates.

## Bottlenecks and Open Research Questions

- Continue development on self-assembly of artificial cells/particles
- Devise methods for the dis-assembling artificial cells/particles – altering properties
- Data needed to validate models – measure properties of artificial networks – elucidate nature and strength of molecular bonds
- Faster more powerful computers



## Goals and Potential Impact if Successful

The broader goal is to develop technology for assembly of the micro- and nano-scale analogs of printed circuit boards. This will require placement of many different types of tiny components on the same substrate and interconnecting them in some way. An example today is a DNA chip where many different DNA strands act as tiny devices that together quantify genetic expression or point mutations.

Potential impact includes:

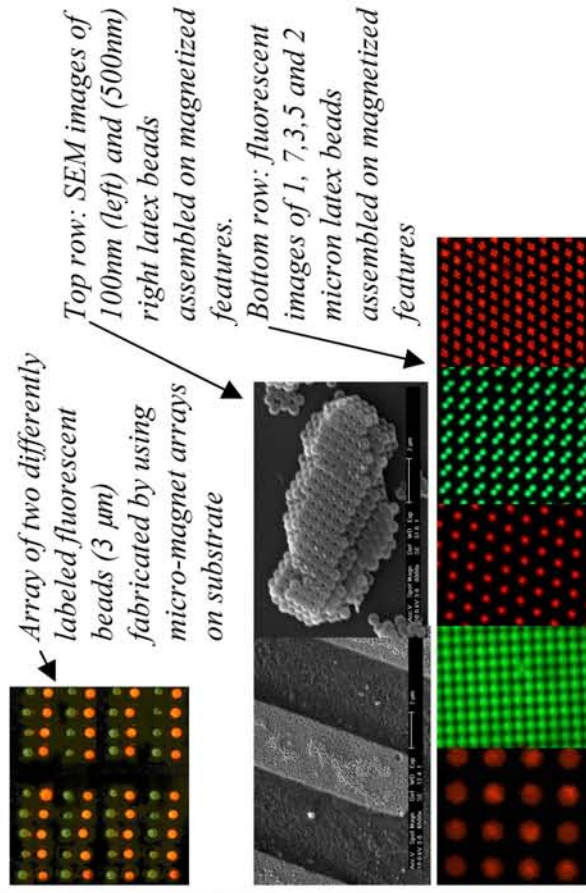
- increased functionality resulting from integration of electronic components, molecular components, fluid handling components, heating components and others.
- increased sensitivity and reduced cost that comes with reduced system size

## Approach and/or Accomplishments

**Our approach is to use magnetic information recorded on a substrate to control placement of components such as molecules, nanoparticles and micro-chips.**

We have demonstrated:

- 1) That programmable placement of magnetic particles is possible
- 2) That programmable placement of non-magnetic micro- and nano-particles of spherical and rod-like shapes is possible
- 3) that molecules such as biotin, streptavidin can be concentrated at designated sites on a substrate in a programmable fashion.
- 4) That magnetic and non-magnetic material can be moved on substrates using mechanism of magnetically actuated Brownian ratchet
- 5) That fluid can be agitated by magnetic micro-stirring in programmable locations



## Bottlenecks and Open Research Questions

- 1) What is the ultimate placement accuracy? This accuracy may be limited not only by the placement process, but by physical and chemical stability of the final system. Since magnetic recording is being used to program placement, what are the optimal strategies for such recording? Can systems be designed to tolerate some placement inaccuracy and some time-variability?
- 2) What are the computationally tractable strategies for modeling the assembly process? One of the key problems is computing long-range interactions and we are working on special multi-scale methods. Since different types of components are being assembled, no single dominant physical force may be controlling the process.
- 3) Can near real-time process monitoring be performed? This is important in controlling the process and knowing the product quality. We are considering x-ray techniques for nanoparticles. Can functional testing techniques be devised?



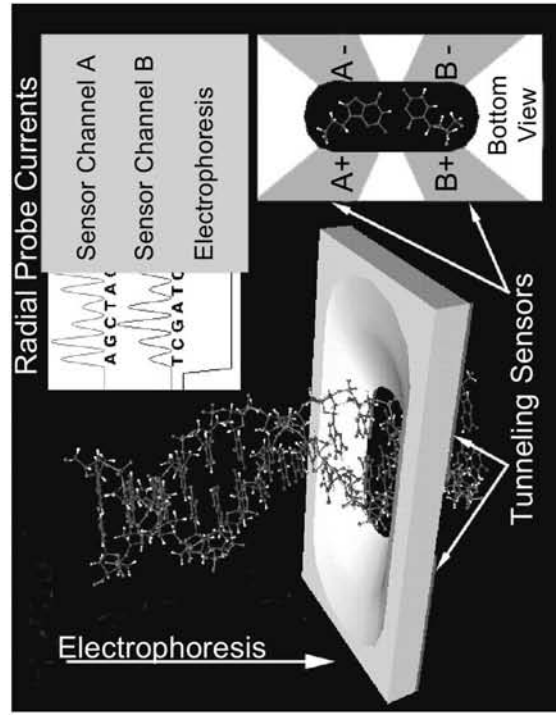
## Radial Probe DNA Sequencing

### Goals and Potential Impact if Successful

Sequencing 90% of the DNA in the human genome is a tremendous accomplishment but the full potential of DNA sequence data will only be realized when multiple human genomes can be completely, rapidly, and inexpensively sequenced. This goal remains impossible with existing sequencing methods. SeiraD is developing a sequencing instrument using molecular level sensors. SeiraD's Radial Probe Sequencing approach has the potential for reducing the cost of sequencing an entire genome from millions to hundreds of dollars while reducing sampling time from years to hours. The approach incorporates double stranded DNA, eliminates enzymes and size fractionation, and tremendously simplifies the sequence assembly problem.

### Approach and/or Accomplishments

The Radial Probe DNA Sequencing concept is illustrated above. The left-hand image shows the probe with double-stranded DNA passing through the pore. The lower right hand image is a bottom view of the probe with a DNA base pair between the sensors. The upper right hand image is a depiction of radial probe data. The smallest dimension of the funnel shaped pore is approximately  $15\text{\AA} \times 30\text{\AA}$ . Electrophoresis current drives the DNA through the pore and the tunneling sensors resolve individual base pairs. The base pair lowers the tunneling barrier and tunneling current increases. The 2:1 aspect ratio of the pore prevents DNA from rotating in the pore and enables the two sensor channels to simultaneously monitor both strands of the double-stranded DNA. Differences in the electronic structure of the DNA bases are expected to result in characteristic tunneling signatures for the DNA bases.



### Bottlenecks and Open Research Questions

SeiraD's pore production and nanolithography processes are limited to single die. Registering the nanolithography with the pore is also problematic. The transition from nanolithography write lines to standard optical lithography patterns is currently accomplished using FIB. This is also a single die process. The fundamental question that remains unanswered is "Will the bases be distinguishable using tunneling currents?" Factors that may impact the tunneling currents include tunneling contributions from the solution and support matrix, electronic diffusion in the DNA, and sensor geometry.

## Goals and Potential Impact if Successful

Development of Nanofluidic Molecular Sieves and Filters for Biomolecule Separation, as an alternative of random, nanoporous molecular sieving materials

- Molecular sieving by regular nanostructures (precise control and optimization possible)
- Better robustness than polymeric nanoporous materials
- Easier Integration into higher-level BioMEMS devices

### Potential Impacts

- (1) Smart nanofluidic molecular filter that can replace porous membranes in diverse applications
- (2) New molecular transport phenomena at the nanoscale could lead to better molecular sieving / filtering / control

## Approach and/or Accomplishments

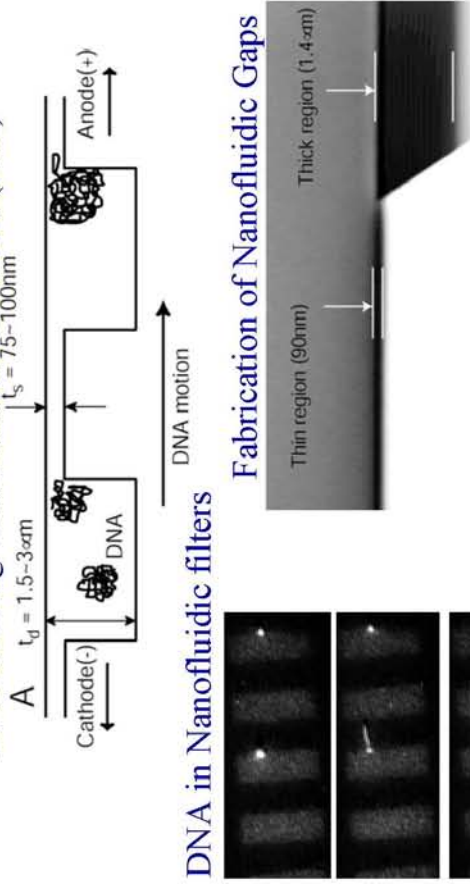
### Development of Nanofluidic filters

- Fabricate nanofluidic molecular filter devices with 10-100nm critical dimension
- Test molecular separation techniques based on the hindered transport of various biomolecules, including proteins and DNA.

### Study of molecular stochastic motion at nanoscale

- Study the molecular stochastic motion in nanochannels (10-100nm) using fluorescence correlation spectroscopy (FCS)
- Investigate the effect of Debye layer thickness, hindered transport of molecules in confined space

## DNA Sieving with Nanofluidic Filters (Han)



## Bottlenecks and Open Research Questions

- Computational (stochastic) modeling of molecular transport through nanofluidic filters or similar-sized molecular sieving systems : Continuum-based modeling generally breaks down at this size scale, and computationally expensive methods are sometimes required.
- Characterization of ultra-thin nanochannels: Roughness, Thickness, Surface Chemistry (or control of it)
- Science of molecular diffusion / transport in small dimension is not clear yet



# Fabrication of Precision Self-Assembly Nanostructures

Michael J. Heller  
University of California, San Diego

## Goals and Potential Impact if Successful

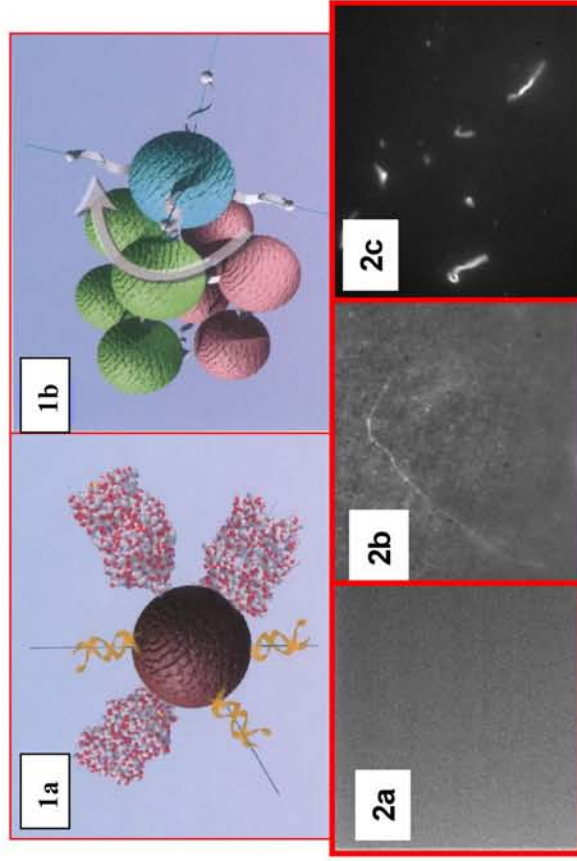
The primary objective is to develop new science and technology for making precision nanostructures which can self-assemble into higher-order structures and devices. The work focuses on discovering synergies between top-down and bottom-up processes in order to develop “viable” nanomanufacturing techniques.

Such new nanofabrication processes may have a broad impact on nanotechnology by leading to cost effective manufacturing for a new generation of more complex structures /devices, not possible with current fabrication techniques. Additionally, we look to biology for better understanding of “molecular to nano to micro” scaling issues; to the biological hierarchical self-assembly processes; and to the utilization of high fidelity recognition molecules (DNA, proteins, etc.) for nanofabrication purposes.

## Approach and Accomplishments

An electronically addressable pick & place platform is being developed to carryout the selective and high precision functionalization of nanocomponents (figure 1a). Such precision functionalization of nanostructures is a prerequisite to subsequent self-assembly into higher-order 2D and 3D structures (figure 1b)

Stoichiometric methods were used to selectively functionalize quantum-dots with DNA sequences, where the DNA sequences were oriented in roughly polar positions. Hybridization of two sets of Q-dots with complementary DNA produced some long linear assemblies of DNA Q-dots. (Figure: 2a – non-assembled DNA Q-dots; 2b – linear assembly of DNA Q-dots (>10 um) ; 2c – shorter linear assemblies of DNA Q-dots. Results represent a first level of success for selective functionalization and self-assembly of linear higher-order structures.



## Bottlenecks and Open Research Questions

While certain methods, such as stoichiometric functionalization, can be used to demonstrate potential for self-assembling nanostructures, these techniques are probably not viable for making precision nanostructures in reproducible and cost effective manner.

Viable nanofabrication processes (such as electronic pick and place platforms) must be developed to carry out the selective precision functionalization of nanocomponents for subsequent self-assembly into higher-order 2D and 3D devices and structures. Present nanofabrication methods do not allow most nanocomponents (quantum dots, photonic crystals, fluorescent polymers, metal and ceramic nanoparticles, nanotubes, etc.) to be modified in a controlled, precise, and cost effective manner.

# Microfluidic Microincubators for Cell Culture

Noo Li Jeon  
UC Irvine

## Goals and Potential Impact if Successful

- to fabricate integrated microfluidic microincubator for applications in cell migration and neuroscience research.
- to have feedback control of cellular microenvironment with fluidics and biosensors.
- design of functional microfluidic devices for fundamental biological research and/or drug screening.

## Approach and/or Accomplishments

### Cell Migration

- microfluidic gradient generation.
- neutrophil chemotaxis in IL-8 gradients.
- cancer cell migration in EGF gradients for >24 hours.

### Neuroscience

- successful culture of primary cortical neurons for 21 days inside a microfluidic device.
- fluidic isolation of soma from dendrites.

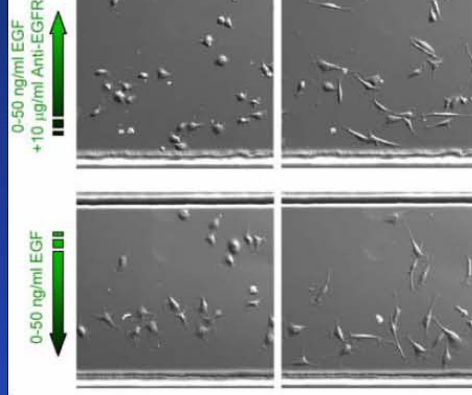


Figure 1. Migration of metastatic breast cancer cells, MDA-MB-231 in soluble gradients of EGF and anti-EGFR antibody.

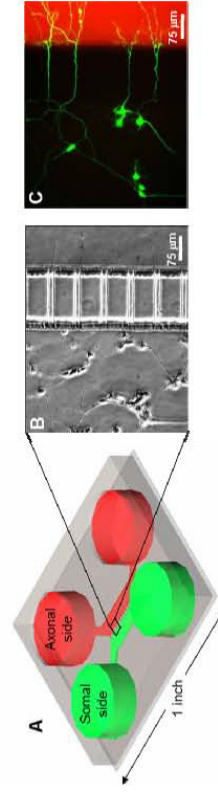


Figure 2. A schematic of the microfabricated device for simulating microenvironments encountered by neurons in the brain (A) and the characterization of this device (B-C).

## Bottlenecks and Open Research Questions

- Integration of biosensors-i.e. oxygen and temperature.
- On chip integration of temperature control/heaters
- Integrated valves and pumps for recirculating media

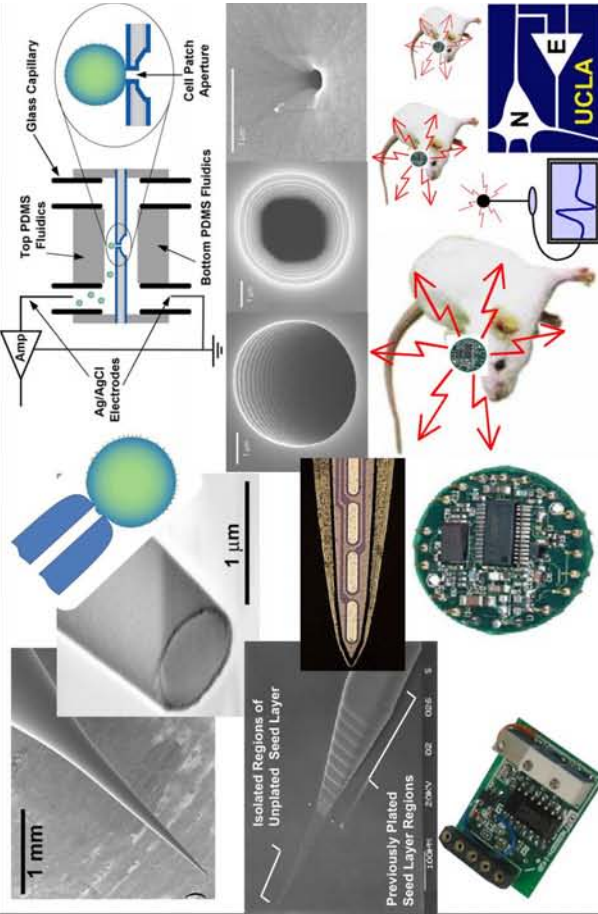


## Goals and Potential Impact if Successful

- Use Micro/Nano fabrication to produce MEMS/NEMS that enable new neuroscience or improve productivity
- Brain research is frequently technologically limited
  - existing techniques are effective but *slow / inefficient*
  - most neuroscientists cannot advance techniques much
    - unaware of alternatives, lack training, and resources
- MEMS/NEMS technology can make significant impact
  - micro/nano-scale sensors, actuators, and systems
    - directly monitor and control at all levels of scale:
      - molecular, organelle, cellular, and systems of cells
  - combine with *closed-loop control* for more impact
- Understanding the brain is the next “*Grand Challenge*”
  - long-term and multidisciplinary research area
  - NSF is the agency to enable this area of technology

## Approaches and Accomplishments

- Micro/Nano Systems for Intracellular Interface
  - integrated nanomachined structures with a microfluidic system to monitor real-time cellular physiology
- Microtechnologies for Interfacing with Deep Brain Regions
  - deep brain regions provide regulation and control
    - fine motor control, metabolism regulation, emotions, ...
  - existing technologies (cortical probes) not sufficient
    - longer, more accurate, less damage, multielectrode, ICs
- Integrate Bi-Directional Wireless Telemetry Technology
  - studies with direct-wired connections have limitations:
    - restricts movement, limits behavior, limits experimental duration, prevents socialization \_ *changes outcomes?*
  - wireless sensor technology has advanced considerably
    - TinyOS-based animal-mounted platform developments
    - COTS technology for low-bandwidth applications
    - high-bandwidth platform being studied – *high demand*



## Bottlenecks and Open Research Questions

- Unreliable Cellular Connection (so-called *gigahm seal*)
  - conventional pipettes work but are not understood
  - complex materials, surface-chemistry, biology issue
    - collaborations are required to break up this “log jam”
- Batch-Fabricated 3-D Microelectrode Probe Arrays
  - current methods yield 2-D microelectrode array or require complex assembly to obtain full 3-D array
  - integration of microfluidics would be very beneficial
  - probe material should be stiff during implantation and flexible after implantation (reduce artifacts & damage)
    - new fabrication concepts and resources are needed
- Chip-Scale, High-Speed, Low-Power, Wireless Platforms
  - current focus is on large networks of inexpensive low-bandwidth sensor nodes that are not small enough
    - NeuroMEMS needs a smaller, faster, smarter platform



# Automation of Yeast Pedigree Analysis

John Koschwanez  
University of Washington

## Goals and Potential Impact if Successful

### MANUAL YEAST PEDIGREE ANALYSIS:

- A yeast cell buds every 90 minutes. A researcher manually picks every daughter cell off a mother cell for up to 100 budding events (150 straight hours in the lab).
- Daughters are analyzed to study genomic instability as the mother cell ages.

### AUTOMATED YEAST PEDIGREE ANALYSIS:

- Goal is to perform analysis on 10 to 100 mother cells in parallel.
- A microfluidic system will hold a mother yeast cell in place. Each time it buds, the daughter will be sent to a designated location on an agar plate for further analysis.

## Approach and/or Accomplishments

### SENSING:

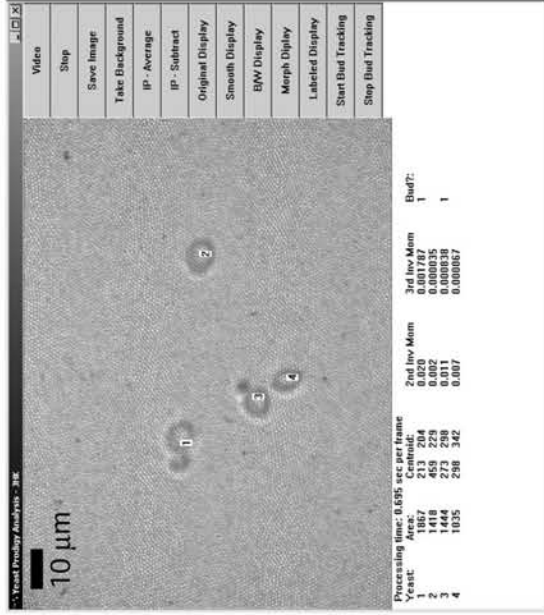
- The optical system uses a fiber-optic imaging bundle - this will allow multiple points on the device to be monitored in parallel.
- Yeast detection and classification of bud status is performed using image processing software. Results in press at *Review of Scientific Instruments* (J. Koschwanez *et al*).

### MICROFLUIDIC DESIGN:

- New designs are built and tested within two days using SU-8 / PDMS fabrication technique.

### SYSTEM INTEGRATION:

- Control software was written in C++ to allow easy integration as each module is designed.



Automatic yeast cell budding classification using image processing software and a fiber optic imaging bundle.

## Bottlenecks and Open Research Questions

- Integrating macro devices, such as electromagnets, into a microfluidic device using a rapid fabrication technique.
- Quickly and inexpensively making a poly or glass surface inert to protein adsorption.
- Achieving 100% success rate with fabrication of microfluidic valves.



# Microfabricated Scanning Endoscope

Per Reinhall and Weichih Wang  
Dept. of Mech. Engr., University of Washington

## Goals and Potential Impact if Successful

The goal of this research is to develop an inexpensive micro fabricated integrated optical scanning endoscope/display system:

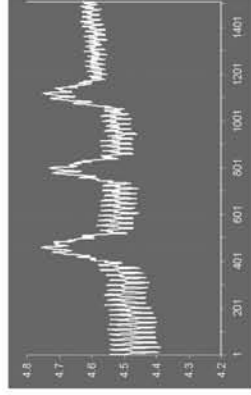
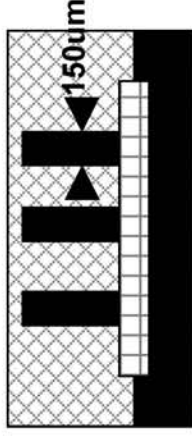
High frequency > 20 kHz sVGA

Large field of view (>90°)

Color

Small (<1mm diameter enclosure)

The small size will enable users to examine areas anatomically inaccessible by currently designed endoscopes and enable integration of imaging with other functional devices such as therapy and diagnostic devices.



## Approach and/or Accomplishments

### Modeling:

Use of nonlinear dynamics to understand the behavior of the scanning wave guide. Whirling, harmonics and bifurcations.

Use of finite element modeling to increase reliability.

### Experimental work:

Construction of prototypes have shown feasibility. So far: Epoxy resin based cantilever waveguide scanner, 30° field of view, greater than 5kHz, stable scan.

## Bottlenecks and Open Research Questions

**Optics** - Light coupling efficiency, diffraction limit, micro lenses, optical properties.

**Material Data** - Mechanical and optical loss factors, fatigue life, etc.

**Integration and Packaging** - Complexity in fabricating integrated systems. Durability and compatibility in a clinical setting

**Control** - Closed loop control may be necessary for large displacements of scanner. Endoscope manipulation to reach hard to reach areas.



# Integrated Platform for Biomedical Implants

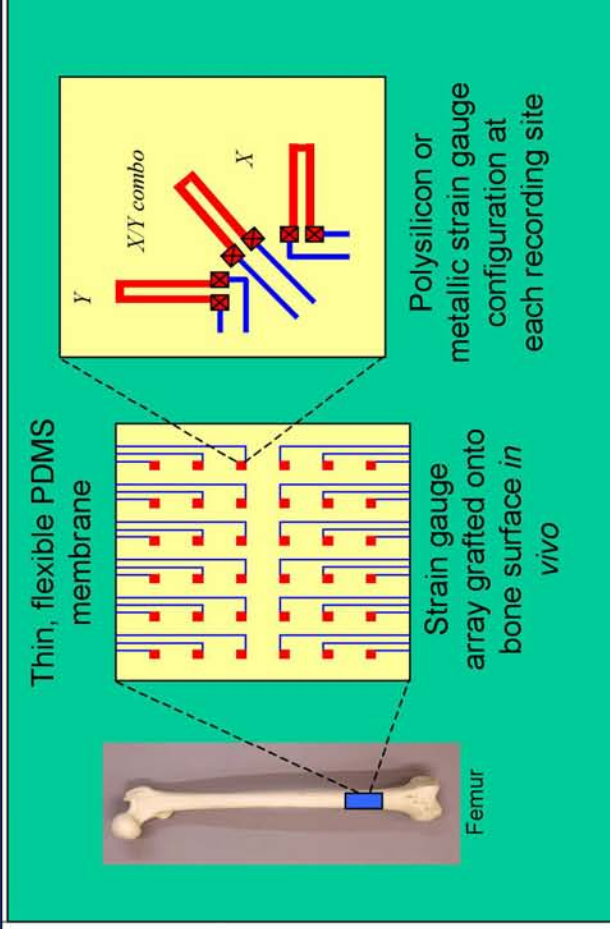
William C. Tang  
UC Irvine

## Goals and Potential Impact if Successful

The goals are to (1) develop novel polymeric and biomolecular assembly processes; (2) create novel polymeric *in-vivo* biosensors with the developed processes; and (3) integrated system design for ultra-low power operation and wireless data and power transmissions. The potential impact if successful is the creation of an enabling platform for a broad variety of biomedical implants, including sensory organ augmentations and replacements such as cochlear and retinal implants, neural implants for Parkinson diseases, implanted real-time physiological monitoring instrumentation, closed-loop bio-sensing and therapeutic deliveries, and *in-vivo* physiological research.

## Approach and/or Accomplishments

Several materials systems will be studied extensively for both biocompatibility and ease of fabrication and integration. PDMS is one of the prime target materials for research, in addition to other polymeric materials. First novel device to demonstrate this integrated platform is an implantable strain-gauge array on a PDMS substrate for research in mechanical characteristics of bone samples, and ultimately for real-time stress-strain data collection on bone surfaces for post-surgery monitoring. Ultra-low-power circuit strategies will be explored, together with wireless power delivery to eliminate on-board batteries. Ultra-low-power wireless data transmissions are also part of the research thrust. Finally, total system integration techniques will be explored.



## Bottlenecks and Open Research Questions

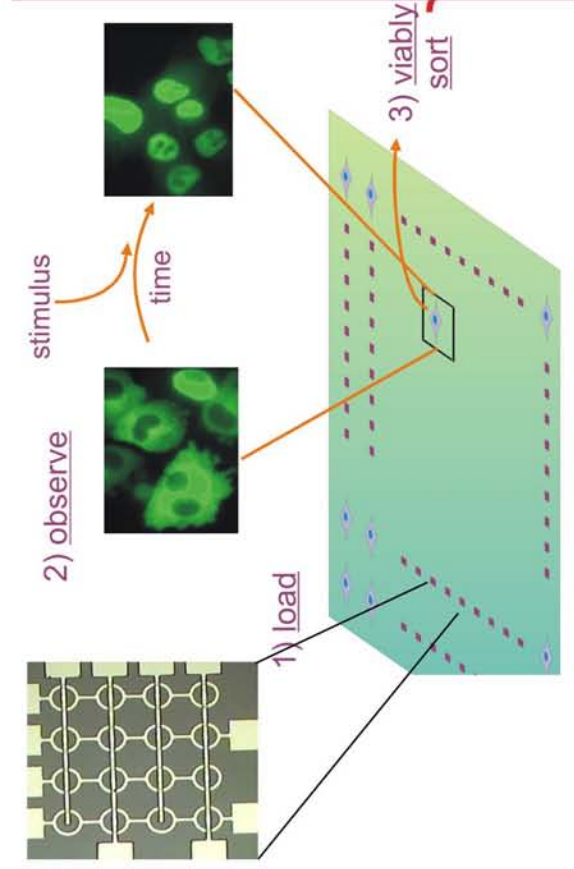
Biomedical implants operate in an environment that uniquely challenges all aspects of engineering and materials integration. The obvious needs for drastic device miniaturization, functional integration, and significant power reduction lend themselves to MEMS technology. Significant extension of the existing MEMS tool sets and materials basis are needed, particularly on non-silicon based materials and processes for bio-compatibility while retaining the advantages of batch fabrication and integration. The systematic understanding and disciplined development of novel bio-compatible materials and their use in device designs are lacking, and therefore present a unique opportunity to research for micro implants.



## Microtechnology for cellular measurements

### Goals and Potential Impact if Successful

- Goal: to create microtechnology that can acquire novel information from cells
  - to build models of cell function
- The potential impact is to aid in understanding biological systems
  - Drug discovery
  - Human health
  - Basic biological science



### Approach and/or Accomplishments

- Our approach is to use extensive modeling to predict performance *before* fabrication
- This is what enables design of non-intuitive structures that can meet complex system needs
- One example in figure
  - A cytometer that can image and then sort cells
  - Uses electric fields—dielectrophoresis—to manipulate cells
  - Combines functionalities of microscopy and flow cytometry
  - Enables new analyses of spatial/temporal cell processes

### Bottlenecks and Open Research Questions

- System-level approaches to working with cells
- Reliable operation with many cells is *the* biggest challenge
- Need protocols, surface treatments, design approaches that are tolerant to the immense biological variability
- Interactions of cells and microsystems
- Genome-wide and molecular analysis of artifacts
- Modeling tools
  - That are fast enough to be able to *design* devices involving liquids, electric fields, and particles
- Materials
- Non-fluorescent photopatternable polymers

# Electrokinetically-Driven Complex Flows in Microchannels

Yitshak Zohar  
University of Arizona

## Goals and Potential Impact if Successful

- Microchannel liquid flow is dominated by surface forces resulting in **laminar** and **stable** flow (low Re)
- Utilize a surface force, **electrokinetics**, to generate any arbitrary micro flow pattern using **patterned surface charge**.
- Apply this approach to realize complex liquid flow for **mixing of liquids in a microchannel**.
- **Fine control of liquid flows** on a microscale, in terms of magnitude and direction in simple geometry.
- Achieve **efficient mixing** of liquids on a microscale
- Utilize this approach in **Bio-MEMS applications** such as the lab-on-a-chip concept.

## Approach and/or Accomplishments

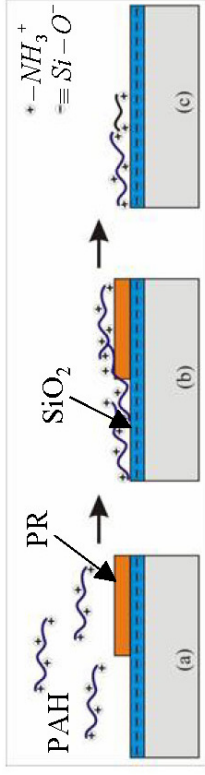
### TECHNOLOGY

- Develop surface chemistry technology based on polymer coating to selectively pattern the surface charge to be either positive, negative or neutral, using standard techniques.
- Develop fabrication technology to realized complex liquid flows in microchannels.

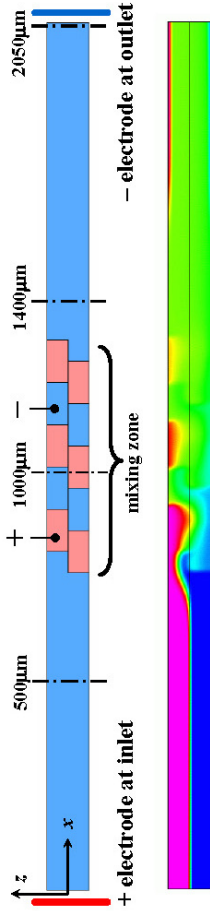
### MODELING

- Develop theoretical models and numerical schemes to analyze these micro fluidic systems.
- ACCOMPLISHMENTS**
- **Bi-directional, in-plane and out-of-plane vortical motion** have experimentally been demonstrated, under a single driving force, confirming theoretical and numerical results.

## - Schematic illustration of the surface chemistry technology



## - Simulations of mixing of two liquids in a microchannel



## Bottlenecks and Open Research Questions

- Characterization and limitations of the polymer coating technology; stability over time, sensitivity to ambient conditions such as temperature; interaction between the polymer coating and the working liquids; etc.
- The creation of areas with no surface charge, i.e. neutral, is still problematic.
- How to create gradients in the magnitude of the surface charge?
- How to create time-dependent surface charge in both sign and magnitude?
- How to protect the polymer coatings from corrosive liquids while maintaining the original surface charge?

### ***Control Systems with a MEMS and/or Nano Perspective***

John Birdwell, The University of Tennessee .....	42
Jason Gorman, National Institute of Standards and Technology.....	43
Carl Knospe, University of Virginia .....	44
Mayuresh Kothare, Dept. of Chem. Eng., Lehigh University.....	45
Robert M'Closkey, UCLA .....	46
Kameshwar Poolla, UC Berkeley.....	47
Harshad Sane, Corning-IntelliSense.....	48
Benjamin Shapiro, University of Maryland .....	49
Marwan Simaan, University of Pittsburgh.....	50
Metin Sitti, Carnegie Mellon University .....	51
Mikhail Skliar, University of Utah.....	52
Tzyh-Jong Tarn, Washington University .....	53
Marc Weinberg, Draper Laboratory .....	54
Takis Zourtos, Texas A&M University .....	55

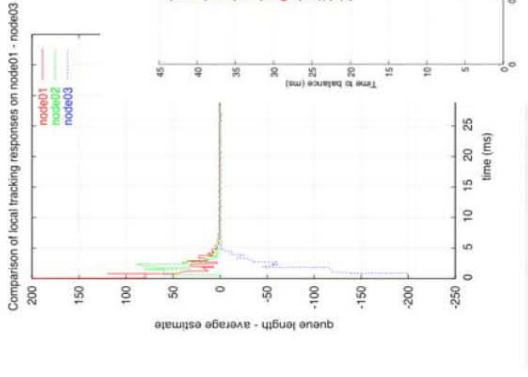


# The Impact of Time Delays in Interconnected Systems

Doug Birdwell  
The University of Tennessee

## Goals and Potential Impact if Successful

- Improved understanding of limitations imposed by time delays in decentralized control system applications.
- Improved operation of distributed and parallel computing and networking systems, with specific applications in load balancing and dynamic resource allocation.
- Development of modeling and analysis methods for distributed control systems, including performance and stability analysis.



Impact of control gains on performance and transient behavior of load balancing.

## Approach and/or Accomplishments

- Developed several decentralized control methods for load balancing in parallel computing
  - Modeling using continuous state / continuous time models.
  - Proof of stability and model consistency.
  - Experimental work using (a) parallel computing cluster, (b) peer-to-peer wireless networking, and (c) wide area computer networks validates modeling approach.
- Examined dynamic resource allocation strategies in the presence of random time delays -- ongoing work.

## Bottlenecks and Open Research Questions

- Modeling approaches include discrete-event, hybrid, and continuous time/continuous state systems. Each has its advantages, but comparison between methods and translation of results from one framework to another is difficult.
- Experimentation is complicated because no single clock exists; data can be gathered, but there are unknown random time skews.
- Time delays in networked systems are random and change on a per-packet basis.

# Micro- and Nano-Scale Assembly

Jason J. Gorman  
NIST

## Goals and Potential Impact if Successful

One goal of the Integrated Nano-to-Millimeter Manufacturing Program is to develop methods and systems which support an integrated approach to control, modify, manipulate and assemble across mm and nm scales. Two manipulation and assembly systems are currently being explored:

### Microassembly using Mechanical Manipulation

- Automated dexterous assembly of hybrid MEMS and optoelectronic devices
- Achieve flexibility and reliability suitable for real world production

### Micro- and Nano-Scale Assembly using Optical Tweezers

- Multi-dimensional assembly of components with complex geometries and varying optical properties
- Applications include nano-scale optical devices and high-bandwidth automated DNA sequencing

## Approach and/or Accomplishments

### Models

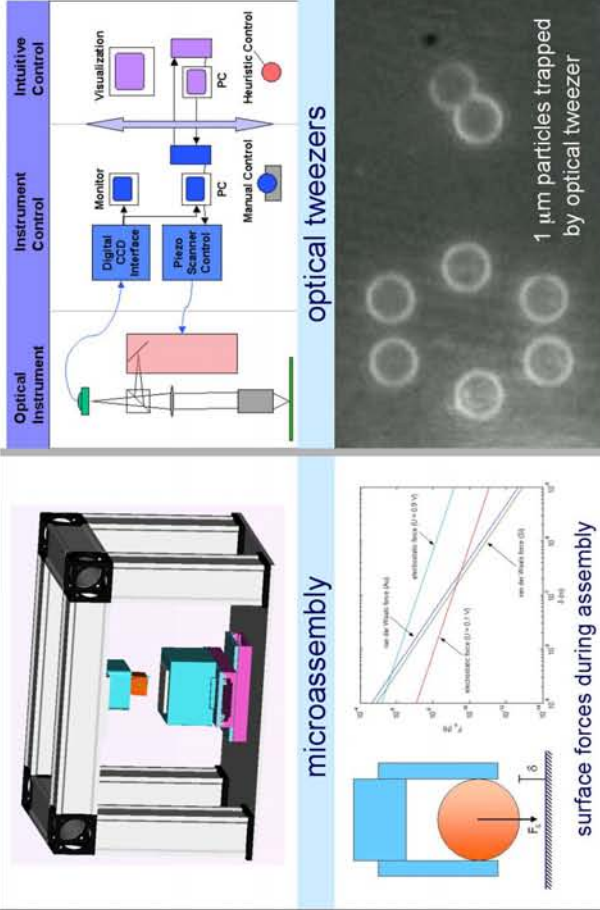
- Integrate macro-scale (robot dynamics), micro-scale (MEMS dynamics, friction), and nano-scale (surface forces) models
- Develop approaches for modeling optical trapping of non-spherical, non-refractive components

### Control Systems

- Utilize combinations of robust and adaptive control to address inherent nonlinearities and incomplete models at the micro- and nano-scales
- Estimation-based controllers due to inferred sensing of processes

### Virtual Interfaces

- Provide model-based feedback of assembly forces and heuristic rules to constrain motions during telemanipulation



## Bottlenecks and Open Research Questions

### Sensors and Sensing Techniques

- There is a need for suitable small robust position and force sensors
- Image processing has severe bandwidth and resolution limitations in tracking the motion of nanoparticles

### Modeling

- Most modeling efforts at the micro and nano-scales concentrate on simple geometries
- 6 DOF models for complex geometries are required, along with model reduction techniques for real-time implementation

### Driving Applications in Nanotechnology

- Applications in nanotechnology will determine which assumptions for assembly are acceptable. However, these applications are not mature enough to provide the necessary feedback.



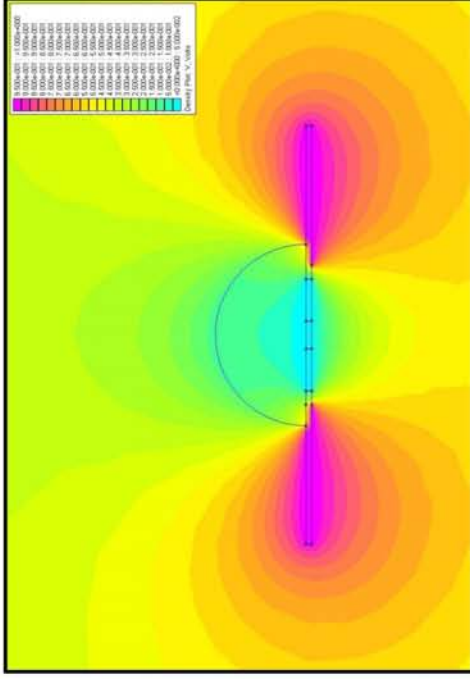
## Goals and Potential Impact if Successful

- Harness surface tension forces to power the movement of microscale droplets and structures. At this scale, surface forces are dominant in determining behavior as gravitational and inertial contributions are minor.
- Engineer active surfaces that enable control of such devices; minimize complexity and cost for sensing, actuation, and control in device design
- Enable fundamentally new approaches to actuation and assembly that are powered by surface tension

## Approach and Accomplishments

- Contact line ratcheting for the rectification of zero-mean motion via surface profile spatial asymmetry to yield directed motion
- Ratcheting enable directed motion without any global gradient in pressure, temperature, electrical field, or surface chemistry
- Ratcheting alleviates sensing and control burden
- Analysis via analytical /numerical approaches

(Collaborator: H. Haj-Hariri, University of Virginia)



Actuator design: electrical potential in 100  $\mu$  drop on ratchet

## Bottlenecks and Open Research Questions

- Modeling: developing models appropriate for design optimization and control synthesis is difficult because of the multiple scales / multiple disciplines inherent to such devices. Significant retooling for control engineers.
- Control: behavior is highly nonlinear and uncertain. High sensitivity to surface properties may indicate increase variability in operation. Ratcheting useful for managing uncertainty?



# Integrated microchemical systems for fuel processing applications

Prof. Mayuresh Kothare, Khaled Al-Fadhel, Leonidas Bleris, Samrat Mukherjee and Ashish Pattekar

CHEMICAL ENGINEERING  
PC BOSSIN COLLEGE OF  
ENGINEERING & APPLIED SCIENCE

## A microreactor for methanol reforming

- Catalytic methanol steam reforming for hydrogen production
- Hydrogen delivery system for PEM fuel cell power systems

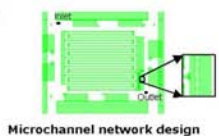
Reaction Scheme: (Using Cu/ZnO/Al<sub>2</sub>O<sub>3</sub> as catalyst)



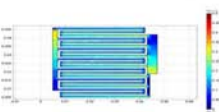
20 Watt Fuel Cell → 0.3721 gmol/hr H<sub>2</sub> flow rate

0.1536 gmol/hr methanol at 85 % conversion

2.038 Watt power required for endothermic reaction



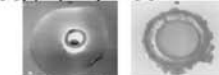
Microchannel network design



Simulation results: gas flow velocity magnitude (m/s)



SEM image of interconnect (a) (Epoxy side) and (b) Channel side



Pattekar, A., and M. Kothare, Novel microfluidic interconnects for high temperature and pressure applications. *Journal of micromechanics and microengineering* 13:337-342 (2003)



SEM image of microchannels/filter



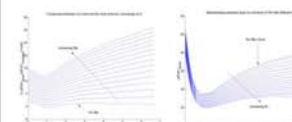
## Mathematical Modeling of Membrane Microreactors

### Modeling Challenges

- Unique geometry (full dimensionality)
- Coupling between momentum, heat and mass transfer
- Large degree of non-linearity (reaction, permeation,...)
- Significance of secondary effects (slip, temp. jump,...)
- Physics of microchemical systems is not well understood

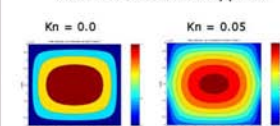
### Microfluidic Flow:

- Study the effects of size reduction
- Incorporate permeation & velocity slip
- Provide analytical expression for (ΔP)
- Excellent link to previous work

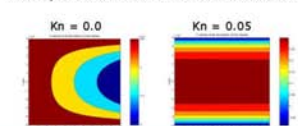


### Effects of Knudsen Number:

Cross-sectional Inlet velocity profile

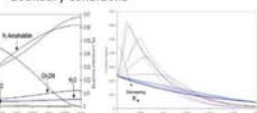


Velocity on the lower surface of the microchannel



### Mass balance:

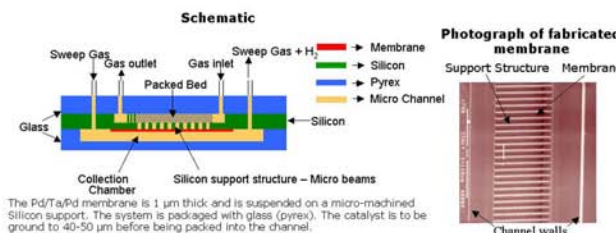
- Simplified general modeling approach
- Addresses non-isothermal & non-isobaric conditions
- Variable volume & non-elementary reversible reactions
- Meaningful concentration profiles with less boundary conditions



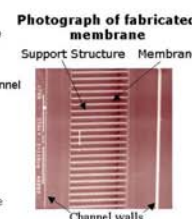
## Design & Fabrication of a Membrane Micro-Reactor

**Goal** – Design and fabrication of a packed bed membrane micro-reactor for the purpose of cleaning up the effluent of the reformer before feeding to the fuel cell. The reformer effluent contains carbon monoxide which poisons the fuel cell catalyst.

The membrane micro reactor consists of a palladium based membrane for hydrogen separation and a commercial packed bed catalyst for Water-Gas Shift Reaction.



The Pd/TaPd membrane is 1 μm thick and is suspended on a micro-machined Silicon support. The system is packaged with glass (pyrex). The catalyst is to be ground to 40-50 μm before being packed into the channel.



### Fabrication Steps



... packaged by anodic bonding glass wafers & connected teflon tubes for micro fluidic connection

## Dynamics and Control of Microchemical Systems

Dynamics: Finite Element Method (FEM) simulations of PDEs  
Control: Distributed Parameter Systems (DPS) control  
Flow, heat transfer, pressure and reaction control  
Controllers for the manufacturing process

Implementation: Need for an efficient embedded controller

### Proper Orthogonal Decomposition (POD)

- Proposed model based controller using POD:
- Obtain the eigenfunctions of the FEM simulation results by means of POD
  - Calculate the desired eigenfunctions
  - Minimize "error" cost by adjusting the boundary conditions under the constraint of invariant eigenvectors (q; denotes temporal or spatial eigenfunctions)



### Hybrid Embedded Model Predictive Controller

Micro-controller hosting:

Hybrid: Controller switches to proportional close to the set point  
Reduced precision and logarithm number system arithmetic are used for the implementation

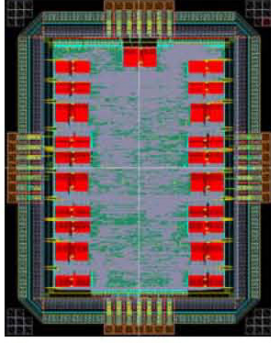
# Modeling, Identification and Control of Inertial MEMS

Robert T. M'Closkey  
UCLA

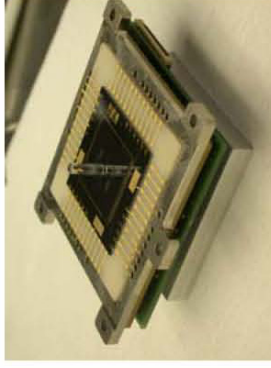
## Goals and Potential Impact if Successful

- Microelectromechanical systems are stimulating the move of modern digital control "on chip" for a growing number of sophisticated applications
- One such application is microinertial sensors of ever increasing capability bring inertial awareness to virtually anything that moves
- Modeling, identification and control of this particular genre of MEMS developed through a Boeing and UCLA collaboration is presented as an illustration on the rising edge of this revolutionary transition in the realization and theory of modern control systems

UCLA ASIC & Algorithms



+



Boeing/JPL gyro

= High performance,  
low cost sensor

## Accomplishments

- Automated tuning of sensor dynamics using ARX algorithms
- Precision frequency response estimates of sensor dynamics using closed-loop identification reveals details of slowly time-varying dynamics
- Analysis and implementation of nonlinear feedback compensation used in this class of devices
- Realization of control and filtering algorithms as a low-power, programmable ASIC that may be configured for individual sensors
- Applications to the Boeing/JPL rate gyros and the HRL Laboratories' electron tunneling sensors

## Bottlenecks and Open Research Questions

- System id methods to support rapid throughput: require models for calibration, tuning and control; each stress different aspects of the sensor dynamics
- Develop alternative control architectures for maximizing performance
- Develop diagnostic tools for pinpointing "nonidealities" during manufacturing process so corrective action may be taken



# Metrology, Modeling, and Control in Nano-scale Manufacture??

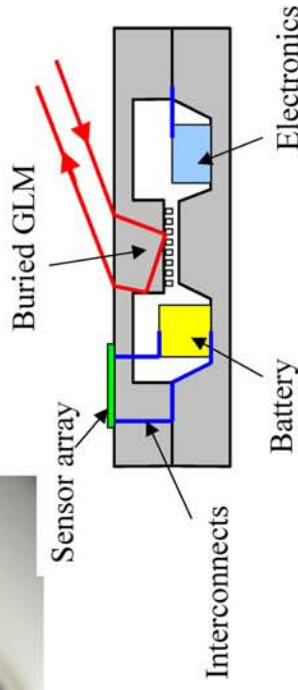
Kameshwar Poola  
UC Berkeley

## Goals and Potential Impact if Successful

Our research has focused on process control and metrology solutions for semiconductor manufacturing. The issues here might well be different than those in nano-scale manufacturing. For example, we believe that tomographic methods at the interconnect level can be used to isolate defects in simple repetitive nano-structures. In the context of this workshop, our goals are to determine the roles of metrology, modeling and control in the manufacture of nano-scale structures and devices.



Sensor arrays for IC manufacture



## Approach and/or Accomplishments

Our approach has been to

- First, build autonomous arrays of sensors using MEMS, standard CMOS, or even thick film techniques
  - Second, to use these sensors to build process models that relate recipe settings to product parameters such as gate CD
  - Third, to use control methods to optimize the processes.
- We have successfully built arrays of sensors to monitor a variety of process variables such as temperature, etch rate, ion density. We have used these sensors to control litho and plasma processes. Our efforts have had commercial success and have been implemented in high-volume production facilities yielding a reduction of across wafer CD non-uniformity by 30% in sub 150nm pattern transfer.

## Bottlenecks and Open Research Questions

- It is very impressive to see that simple repetitive structures of various materials can be made at the nano-scale using self-assembly or other approaches. Interconnecting such structures to form functionally addressable or (better still) programmable devices seems to me a major bottleneck. Reliability, self diagnostics or nano-scale assemblies are other key issue. Can biologically inspired mechanisms be developed to address these challenges? Are there process control challenges? Is it simply too early to examine manufacturing issues for nano-scale devices? Is there a role for tomography or other metrology methods in fault detection and isolation for nano structures?



## Goals and Potential Impact if Successful

Develop robust control strategies for precision control of electrostatically actuated MEMS actuators.

- Applications: micromirrors for optical switching, MEMS accelerometers, MEMS gyroscopes, micromirrors for laser targeting and communication.

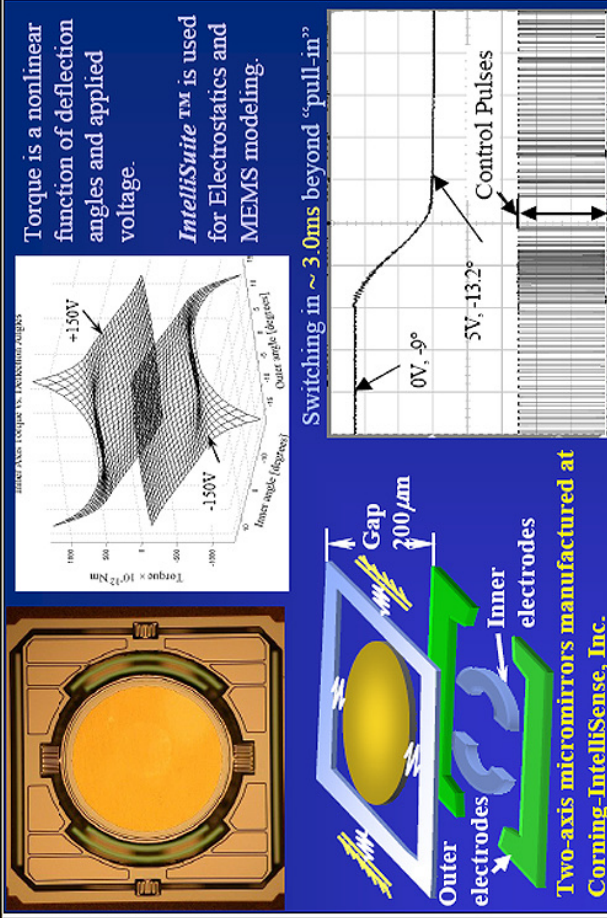
### Practical considerations:

1. Optical switching applications require **high precision** (11bit dynamic range – 5mdeg precision with 15 degrees range)
2. Implementation in **integrated** sense-control circuits to reduce noise, time lags and facilitate scalability.
3. **Robustness** to Lithographic and microfabrication variations in device parameters (could be as much as  $\pm 50\%$ ).
4. Stability and performance over all operational conditions.
5. Fault detection and **drift correction**: humidity, temperature.

## Approach and/or Accomplishments

Discrete-time implementation of a **modified** (adaptive) **sliding mode control** algorithm was successfully demonstrated for **two-axis micromirror** devices for optical switching applications.

1. *IntelliSuite*<sup>TM</sup> used for calculating MEMS dynamical properties. Experimental validation of dynamical models. The dynamical model include out-of-plane translation modes as well.
2. **Sliding mode control** (SMC) provides excellent robustness and a stable operating range of  $\pm 15$  degrees. *Modified* SMC involves adaptive sliding manifold for increased precision.
3. Integrated ASIC sense/control implementation demonstrated. **Capacitive sensing** for angular deflections.
4. Outer loop for temperature/humidity drift compensation.



## Bottlenecks and Open Research Questions

- Algorithms that provide provable stability (Lyapunov based) and robust operation over the nonlinear range. Electrostatic actuation is inherently unstable for large deflections. The linearized dynamics are unstable beyond the pull-in point.
- Feedback linearization, back-stepping and other nonlinearity compensation methods have to address the inherent nonlinearity and the effect of parametric variations.
- Control is not affine. Electrostatic nonlinearity is quadratic. Affine control methods may not be applied for *single-sided* actuation (only positive control inputs).
- Implementation: reliable PWM/PM methods for discrete-time implementation in integrated circuits.



# Modeling and Control of Micro Fluidic Systems

Benjamin Shapiro  
University of Maryland

## Goals and Potential Impact if Successful

- (Feedback) control of micro-fluidic systems such as:
  - Lab-on-a-chip systems
  - Conjugated polymer “conducting plastic” in bio-fluids micro actuators
  - Steering of bio-particles/chemicals in micro-fluidic devices for biological screening, micro drug delivery, etc.
- Create integrated systems that work in messy environments.
- Require feedback on the micro/nano scale for the same reason that it is required on the macro scale: allows systems to function with large degrees of noise and uncertainty, create robust performance, accomplish complex coordinated tasks, integrated sensing/actuation.

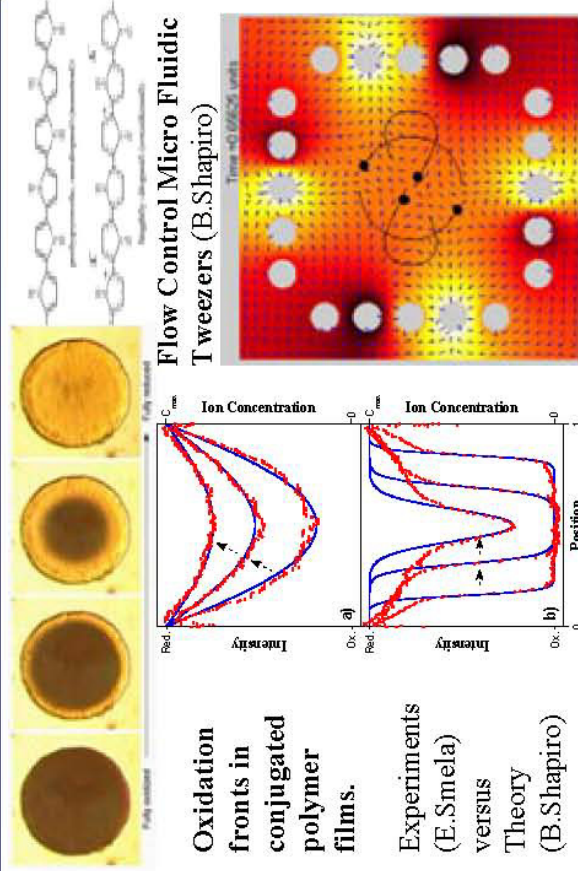
## Approach and/or Accomplishments

### MODELING:

- Identify dominant physical effects by intuition, theory, back-of-the-envelope analysis, experimentation, ...
- Create PDE models of dominant effects. Quantify unknown parameters by careful experiments, system identification, ...

### CONTROL:

- Pose practical tasks (such as split drops precisely using electrically actuated surface tension forces) as tractable mathematical problems (updated least squares control of pinch points).
- Extend/develop PDE control theory to: PDE control on changing topology, non-smooth behavior (interface control) ...



## Bottlenecks and Open Research Questions

- Modeling, analysis, and design tools appropriate for control of micro/nano systems are largely unavailable.**

My lab spends the majority of its time creating control ready models and recreating tools available on the macro scale for the micro scale (such as model reduction tools).

- Communication gaps:** Controls people don't speak the same language as the fabrication people who don't speak the same language as the organic chemistry people who ..

- What are the dominant physics?** Given a complex

bio/chemical system, how do we decide what physical phenomena really matter? Combine knowledge bases?

- System integration:** Design tools. Coupling. Robust nonlinear system ID. Appropriate sensing/actuation. ...

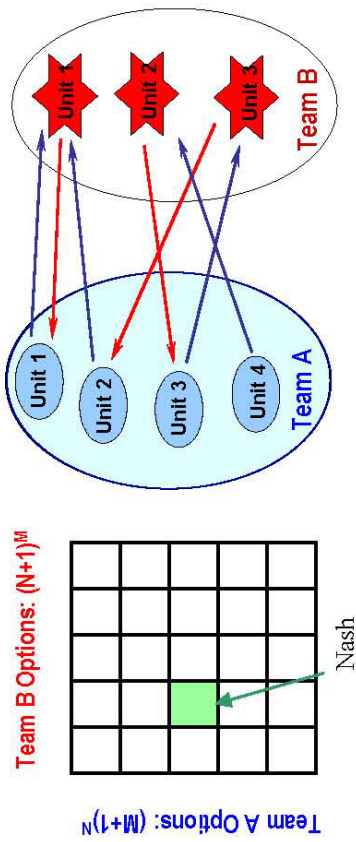


### Goals and Potential Impact if Successful

- Many systems are controlled by a team of controllers that have to operate in unfriendly and often hostile environment. Game theory provides a framework within which such systems can be analyzed and optimized.
- In this framework, the uncertainty due to the environment can be modeled as another adversarial team of controllers with objectives that are in conflict with those of the friendly team.
- The goal is to consider possible mechanisms for describing how the two teams of controllers interact, how eventually the system will evolve, and what the properties of the resulting optimized system are.
- Impact on military, economic, and possibly biological systems.

### Approach and/or Accomplishments

- **An attrition-based discrete time model** describing the interactions between two teams of semi-autonomous entities as they move in a two-dimensional space has been completed.
- **A game theoretic approach** assumes that the adversarial team is intelligent and may be optimizing its actions in the same way the friendly team is. The hostile team might also be using deception techniques to achieve its objectives.
- **A Nash based targeting strategy has been derived.** This strategy assigns to every entity an entity on the other side as a target. The assignment is derived in such a way that a Nash equilibrium is achieved.



# of units Team A	# of units Team B	Size of search matrix	Size of Search Space
4	3	256 X 125	$32 \times 10^3$
8	6	5,764,801 X 531,441	$3.06 \times 10^{12}$

### Bottlenecks and Open Research Questions

- **Adversarial intent and reasoning process:** A major problem that needs to be resolved is how to model the adversary; its intent, and its decision-making process.
- **Model and parameter uncertainties:** not necessarily due to the adversarial team need to be taken into consideration.
- **Structure of information:** In order to address the problem of implementation, assumptions need to be made on who knows what at every instant of time. This is crucial if feedback is to be used to implement the resulting controls.
- **Computational issues:** Scalability becomes an issue as the number of controllers in the system becomes large.



# Micro- and Nano-Scale Robot Design and Control

Metin Sitti  
Carnegie Mellon University

## Goals and Potential Impact if Successful

Development of a formulation for the design, construction and control of micro- and nano-scale robots.

Miniature micro/nano-robots have unique advantages:

- direct accessing to small areas and the micro/nano-scale
- increased flexibility, functionality and robustness
- being low cost, many (swarms), adaptive, and distributed

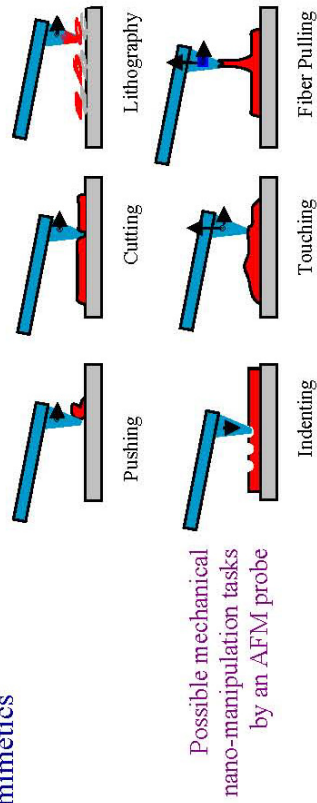
Applications in:

- Health care, biomedical devices, and biotechnology
- Environmental monitoring
- Scientific tools
- Search and rescue
- Inspection, maintenance and repair in extreme environments
- Manufacturing, assembly, information technology, etc.

## Approach and Accomplishments

Overall design methodology specific to the application:

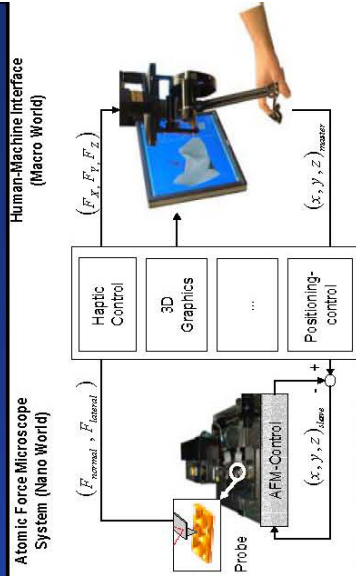
- Micro/nano-scale continuum physics modeling
- Teleoperated and autonomous control
- Atomic Force Microscope probe as a nanoscale robot and sensor
- Rapid prototyping of micro/nano-systems
- Advanced man-machine interfaces
- Biomimetics



3D polymer micro/nano-fiber manufactured by an AFM probe



Biomimetic surgical micro-robots



Augmented reality user interface for AFM

## Bottlenecks and Open Research Questions

- Three-dimensional, parallel, and autonomous nano-manipulation systems are required for nano-material characterization, prototyping novel nano-scale devices, sensors and mechanisms, and mass-produced nano-manufacturing applications.
- New hybrid systems integrating and controlling biological entities and micro/nano-electromechanical systems and using the chemical energy as the power source would be a promising direction.
- Novel realistic continuum model based real-time micro/nano-physics simulators would enable micro/nano-mechanics training and rapid prototyping of micro/nano-systems.
- Miniature nano-scale robots, sensors, and systems would open novel applications in health care, environmental monitoring, search and rescue, biotechnology, wearable devices, self-organizing displays and robots, and desktop size nano-manufacturing system applications.
- Biomimetics could enable multi-functional, robust and smart novel nano-scale sensors, robots, and materials adapting the nature's solutions to the challenging nano-scale engineering problems.
- Advanced human-machine interfaces for nano-scale microscopes, robots, and manufacturing systems are indispensable for direct human control on complex and time-varying applications.

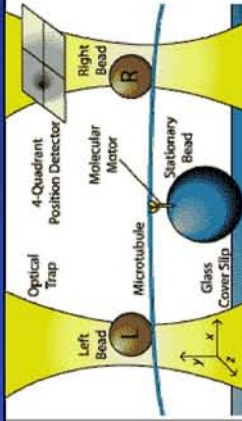


# Monitoring and Control of Bio-Molecular Interactions

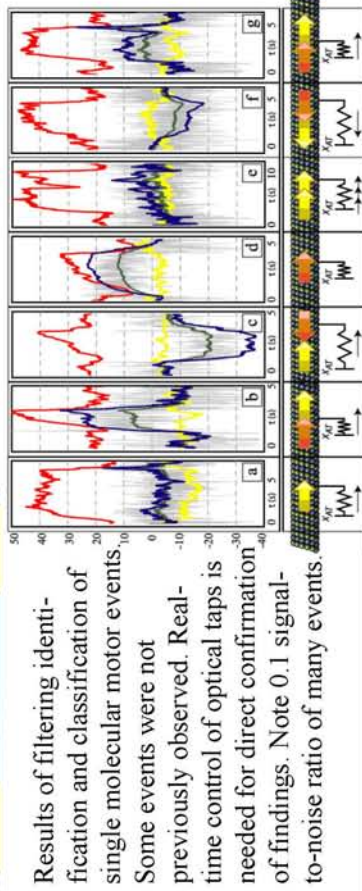
Mikhail Skliar  
University of Utah

## Goals and Potential Impact

Knowledge discovery and the development of nanoscale devices and processes requires the interaction between heterogeneous components of a system and with human operators. A key challenge is the real-time interpretation of measurements obtained from molecular and nanoscale systems. Offline interpretation prohibits automatic control as a function of random nanoscale events. Therefore, there is a need for **real-time, customizable, model-based analysis of measurements on a biomolecular level, their automatic interpretation to detect nanoscale events, and automatic control of experimental conditions to achieve the problem-specific objectives.**



Optical tweezers are used to bring microtubule and Ncd into close proximity. The bead position is measured using a 4-quadrant position detector. Motor attachments and strokes are inferred from position.



Results of filtering identification and classification of single molecular motor events. Some events were not previously observed. Real-time control of optical taps is needed for direct confirmation of findings. Note 0.1 signal-to-noise ratio of many events.

## Approach and/or Accomplishments

- Model-based, single-realization interpretation of biomolecular measurements.
- Use of stochastic models with input, parametric and structural discontinuities.
- We use meso-scale models, which combine the elements of continuums and discrete event models.
- Automatic classification of molecular events is used to characterize molecular interactions.
- Current application: Analysis and model-based interpretation of measurements obtained using optical traps to study the interactions between a single non-processive molecular motor (Ncd) and its complementary filament (microtubule).
- This application indicates a clear need for feedback control to study biomolecular interactions on a single molecular level.

## Bottlenecks and Open Research Questions

- We need to learn how to model processes at the interface of continuum and countable processes.
- The resulting models are likely to be continuous systems with discontinuities. Thus the need for non-smooth analysis and control methods.
- New emphasis on control of stochastic systems (e.g. control on average) is needed.
- Since interface between nano/micro- and macro-level will introduce interferences, it is desirable to process the measurements and generate controls at the source.
- The networking and coordination between multiple nano/micro-devices is needed, which would allow us to instrument and actuate the environment, including that of the human body.
- The research must be multidisciplinary with a strong emphasis on demonstrations.
- High cost of equipment is a problem.



# Dynamics and Control of Bio-nanorobots

T. J. Tarn  
Washington University in St. Louis

## Goals and Potential Impact if Successful

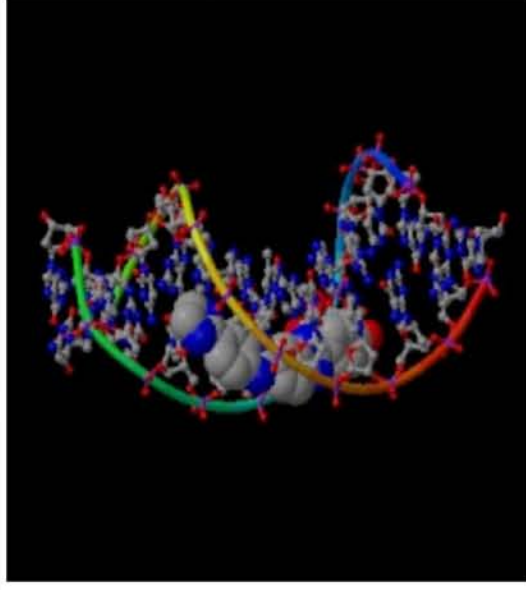
- Find a way to build and control bio-nanorobots.
- Understand nano-scale dynamics: how does a bio-nanorobot handle system dynamics?
- Understand nano-scale control: how is the information being transferred and used for bio-nanorobots?
- Direct impact: nano-medicine and nano-fabrication.**
  - Medicine: better drug design and disease treatment. Man-made bio-nanorobots can be used as vaccines or antibodies against disease.
  - Manufacturing: nano-fabrication for nanotechnology. Bio-nanorobots may be assembled and form multi-degree of freedom nanodevices for nanoworld manipulations.

## Approach and/or Accomplishments

- Mathematical modeling: a correct modeling of bio-nanorobots is the key for understand dynamics and control of bio-nanorobots. Start with ODE model to extend to PDE's.
  - Control: extended application of distributed and decentralized control methods from advanced control theories.
  - Bottom-up fabrication based on quantum mechanical control.
- The author has accumulated many years of excellent research experience in dynamics and control. Solid background and achievements for mathematical modeling and control of dynamic systems including Robotic Systems and Quantum Mechanical Control Systems**

Right figure:

Conformation of B-DNA containing O6-ethyl-G-C base pairs stabilized by minor groove binding drugs



<http://www.rcsb.org/pdb/>

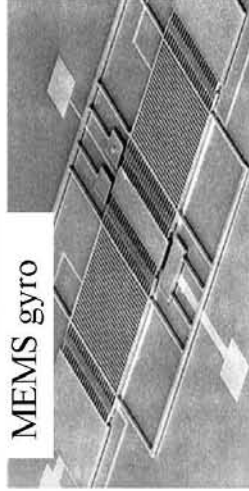
## Bottlenecks and Open Research Questions

- The key is to construct dynamic models at nano-scale.
- **Verification.** Right tools or methods to check accuracy and correctness of the modeling and control. This is a very challenging topic in nano-scale.
- **Implementation.** The difficulty is that it is not known how a bio-nanorobot is controlled, specifically, how to organize bio-molecules to have some kinds of intelligent properties.
- **New physical laws.** Is there any new physical law at nano-scale that can be used for understanding system dynamics and control of bio-nanorobots?

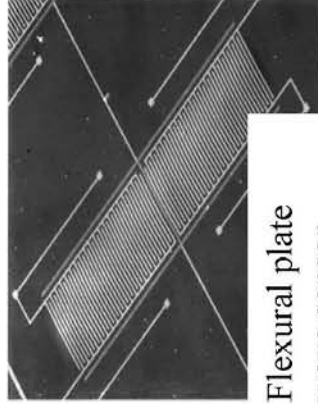
# Sensor Construction, Dynamics, Control, & Applications

## Goals and Potential Impact if Successful

- Design and construct high performance, low power, high acceleration MEMS inertial sensors.
  - Enables military, automotive, and medical applications
- Develop prosthesis to assist balance impaired
  - 40% of US population is effected by dizziness
  - Effects elderly in particular
- Achieve selectivity in chem/bio sensors
  - Enables applications in medical and homeland defense



MEMS gyro



Flexural plate wave sensor



Balance prosthesis sensor package

## Approach and/or Accomplishments

- Developed first and best performing MEMS silicon gyro, which is in commercial production
- Teamed with MEEI to successfully develop control algorithms and demonstrated single axis balance prostheses
- Achieve selectivity in chem/bio sensors with arrays of flexural plate wave, adhesive stress, and microcalorimeters
- Developed code for analysis and design of microthermophotovoltaics (enhanced radiation at small gaps)

## Bottlenecks and Open Research Questions

- Improved gyro and accelerometer performance at high acceleration and shock levels
- Reduced size and power of MEMS sensors.
- Discrimination in chemical sensor arrays
- Demonstration of balance prosthesis over large angles in any direction while standing, walking, and climbing stairs
- Additional applications for MEMS Sensors



# Controller Architectures for Fully-Integrated Micro/Nano-Systems

Takis Zourmos  
Texas A&M University

## Goals and Potential Impact if Successful

**Theme: Sophisticated Control based on Simple Elements**

Goals: 1) develop generic *analog* controller architectures suitable for a diverse range of micro/nano nonlinear systems using basic micro/nano-electronic devices; 2) propose theory and implementation strategies for efficient realization of controllers; 3) identify methods for dealing with substantial plant and controller uncertainty.

## Broader Impact: Facilitate Design of Complex Nano-Systems

*Enable the cost-effective implementation of controlled, single-chip autonomous micro/nano-systems. We specifically address control system complexity and develop both theory and practical techniques to keep hardware cost to a minimum. Please see Figure 1 for the general framework.*

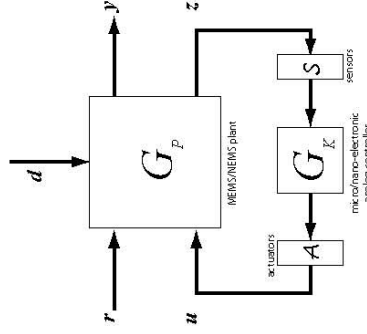


Figure 1: Closed-loop micro/nano-system featuring analog electronic control. A digital control paradigm is generally not suited to full integration of plant and controller.

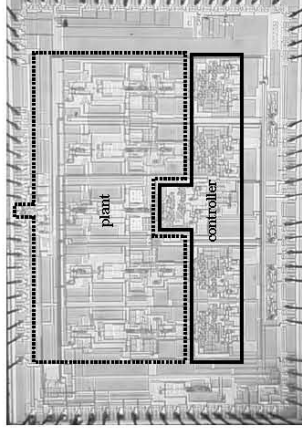


Figure 2: A fifth-order nonlinear control system implemented in a 350-nanometer silicon-based technology. The controller is an analog switching-type design that provides robust stabilization.

## Approach and/or Accomplishments

### Theory

We have developed tunable analog controller architectures for the stabilization of arbitrary-order plants based on low-cost elements using Lyapunov and variable-structure toolsets. Our current aim is the development of low-complexity robust switching controllers for use on nonlinear micro/nano-system models with significant parametric uncertainty.

### Implementation/Experimental Work

We have developed a variable-structure control system in microelectronic form using a silicon-based technology with 350-nanometer feature sizes (shown in Figure 2). We are currently designing controllers using technologies approaching 100-nanometer feature resolutions for electronic systems; experimental verification pending.

## Bottlenecks and Open Research Questions

- 1) How will the choice of substrate material and device structure affect the realization of analog electronic controllers? How should the characteristics of the fabrication technology affect the development of control algorithms?
- 2) What are classes of “important” problems/models with which to address control system research for nano-scale systems? *A clear need exists for dialogue/collaboration between control theory specialists and nano-technology (modeling) experts.*
- 3) Nano-system control identifies a “language barrier” amongst system theorists, modeling experts and experimentalists--- we need to educate ourselves about each other’s fields (which requires considerable effort); how can we facilitate the learning process?

### ***Measurement, Modeling, and Model Validation at the Micro- and Nanoscale***

Ali Beskok, Texas A&M University .....	57
Kenny Breuer, Brown University.....	58
Albert (Terry) Conlisk, Ohio State University .....	59
Martha Gallivan, Georgia Tech .....	60
Thomas Jones, University of Rochester .....	61
Andrew Ketsdever, Air Force Research Laboratory .....	62
Pramod Khargonekar, University of Florida .....	63
James Liburdy, Oregon State University.....	64
Ajay Malshe, University of Arkansas .....	65
Arvind Raman, Purdue University .....	66
Murti Salapaka, Iowa State University .....	67
David Stroud, Ohio State University .....	68
Jacob White, MIT .....	69
Minami Yoda, Georgia Institute of Technology .....	70

## Goals and Potential Impact if Successful

### I. Design of microfluidic systems for

- Concentration, capture and release of microbial contaminants from drinking and recycled water.
- Drug delivery using micro-encapsulated protein micro-spheres.
- Fluid and species flow control and mixing using electrokinetics and chaotic advection.

### II. Colloidal particle aggregation during electrophoretic deposition on patterned electrodes, and dielectrophoresis.

- Particle aggregation in cracks (defects) and constrained geometries — Self healing materials.
- Colloidal self assembly and crystallization.

### III. Microfluidic device control and integration.

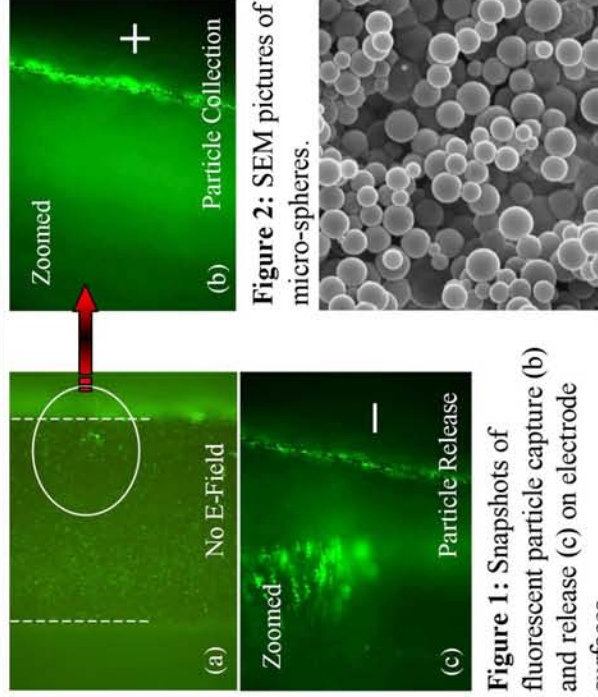
## Approach and Accomplishments

### I. Experiments:

- Proof of concept of bio-particle capture on electrode surfaces is shown in Figure 1. Careful experimentation is planned to investigate capture and particle release.
- BSA & BSA+vpB based micro-spheres prepared using water in oil emulsification. Theoretical correlation to predict average size is developed (Figure 2).
- Experiments to study particle aggregation on patterned electrodes during electrophoretic deposition is underway.

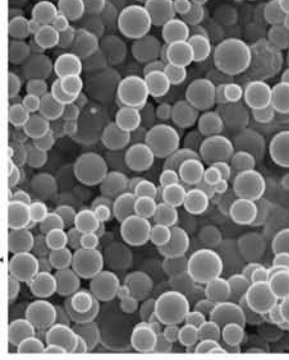
### II. Theory and Modeling:

- Numerical simulation of electrokinetic flows and mixing.
- Particle tracking, chaotic mixing & mixing quantification.
- Theoretical modeling of electrophoretic deposition: Determination of dominant physical effects from experiments.



**Figure 1:** Snapshots of fluorescent particle capture (b) and release (c) on electrode surfaces.

**Figure 2:** SEM pictures of 2 $\mu$ m BSA micro-spheres.



## Bottlenecks and Open Research Questions

### I. Development of theory and numerical models, and validation with experiments

- Identify important parameters that contribute to flow physics from intuition and experiments.
- Electrokinetic transport models involving moving boundaries, realistic particle shapes, particle-particle and particle-wall interactions.
- Model particle erosion and particle diffusion (for drug delivery).

### II. Scale homogenization

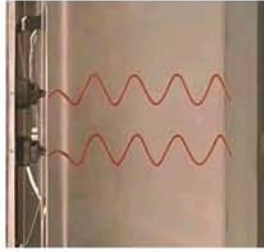
Bridging the gap between the nano and micro-scales and processes, and relate these to macroscopic device/system behavior.



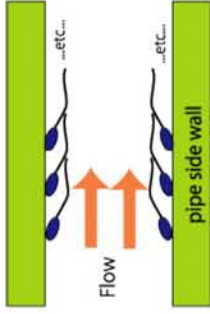
## Goals and Potential Impact if Successful

Understand the mechanics associated with the motility of micro-biological systems – how are forces generated, transmitted, moderated in bacteria. How to they move, how to the sense and control movement? How do bacteria coordinate to accomplish a result that is greater than the sum of their parts?

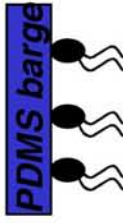
How can we use bacterial components in a controlled engineering environment?



Macro-scale micro-experiments



Baseline mixing      Enhanced mixing



Glass substrate

## Approach and/or Accomplishments

**Modeling:** Develop coupled fluid/structural models for the mechanics of bacterial systems, the behavior of bacterial flagella. Develop analytical and numerical tools for mimicking and predicting the behavior of bacterial systems

**Experiments:** Benchmark experiments on the behavior of bacteria, and bacterial flagella. Macroscopic experiments that mimic microscale behavior. Fabrication of engineered devices that use bacteria in microfluidic applications.

## Bottlenecks and Open Research Questions

Issues at every scale:

- What are the material properties of biological materials (e.g. bacterial flagella, etc)?
- Experimental tools needed to accurately probe living microscale systems at nanometer scale with high spatial and temporal accuracy.
- Fabrication techniques that allow for integration of living systems with engineered systems
- Analytical models that capture complexity without overwhelming computational capabilities

## Electroosmotic and Biomolecular Transport in Micro and Nanochannels

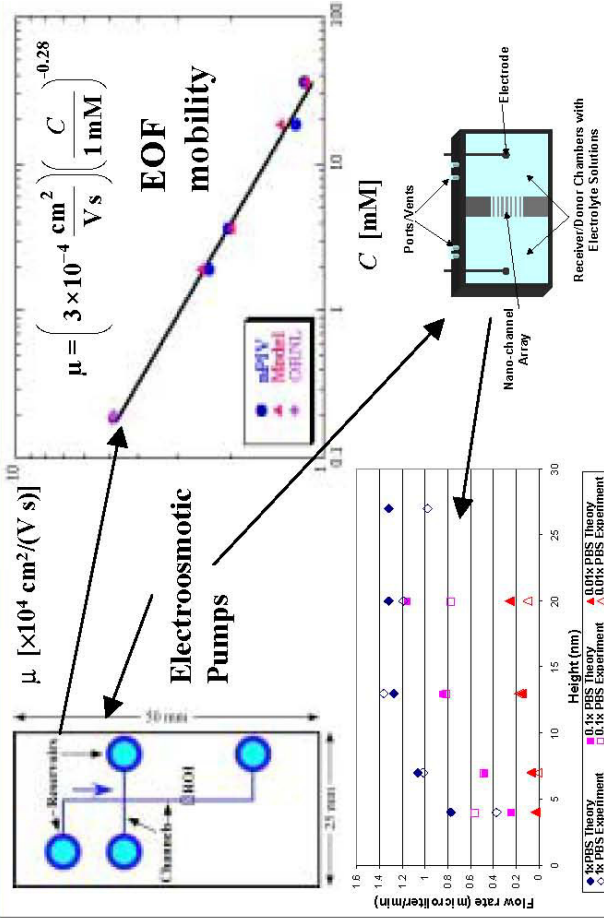
A. T. Conlisk  
The Ohio State University

### Goals and Potential Impact if Successful

- Develop PDE models to predict the velocity profile, flow rate of biofluids through nanopore membranes.
- Develop scaling laws to enable microscale experiments to address nanoscale transport.
- Predict transport of proteins through nanoscale membranes.
- Understand and predict flow effects in unsteady and transient EOF in nanochannels for biomolecular sensing.
- Impact: cut design time of nanoscale devices significantly.
- Reduce the number of prototype devices required.
- Applications: electroosmotic pumps, drug delivery, biomolecular sensing.

### Recent Accomplishments

- Believed to be first published comparisons of model with experiment at nanoscale (Conlisk *et al* AC 2002, Zheng *et al* Electrophoresis, 2003; iMEDD, ORNL).
- Comparison w/iMEDD synthetic ion channel data for glucose and albumin transport very good.
- Tech Transfer: will soon provide iMEDD with suite of EOF programs.
- Completed model for three dimensional flow in 2D confined nanochannels.
- Comparison of model with GTech experimental data extremely good (Sadr *et al* J. Fluid Mech, 2004).
- Summary: Models for ionic and biomolecular transport compare well with four distinct sets of experimental data comprising over 15 operating conditions at micro and nanoscale.



### Bottlenecks and Open Research Questions

- Characterization of surface properties including roughness and charge at nanoscale.
- Properties of biomolecules especially proteins are not well understood. Models need size, net charge, conformation and other properties.
- This information must come from someone with chemistry/biology background.
- Engineers must interface with biologists and chemists routinely. Need a common language base.
- Is there new physics at nanoscale?
- What is the character of the temperature distribution?
- At what dimension does the continuum approximation break down?
- Experimental methods cannot currently address the nanoscale which makes modeling essential.



# Control of Atomic-Scale Process Dynamics

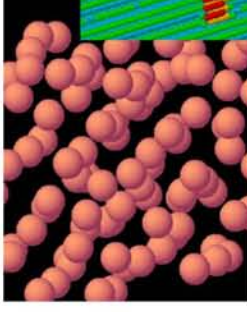
## Goals and Potential Impact if Successful

Goal: to design new materials and devices using predictive models and formal optimization  
 - particularly challenging when the process must be described at the molecular level

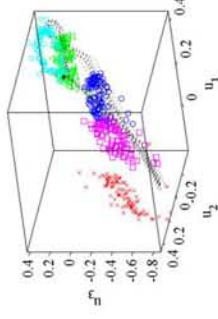
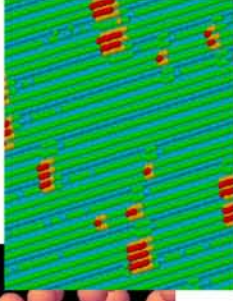
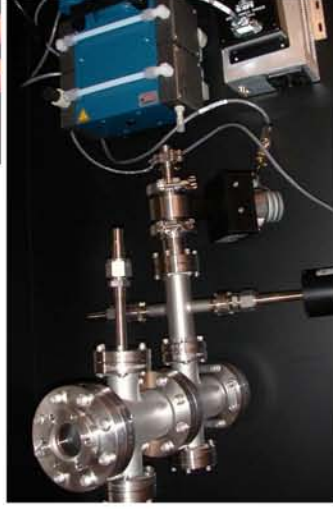
### Examples

- fabrication of integrated circuits
- polymer architecture control in processing

Impact: development of better electronic devices for computing and communications, rational design of advanced materials



- Detailed models
- Reduced dynamics
- Experimental implementation



## Approach and/or Accomplishments

- Identify and focus on industrially relevant problems
- Develop detailed physical models via our own experiments, through collaboration, and through literature models.
- Use standard model reduction algorithms *and* physical understanding to develop more compact process models
- Apply systems tools like optimization and feedback control

**Example**: ultra-high vacuum thin film deposition of Ge

- estimated activation energies in experiment
- developed Monte Carlo and reduced models of morphology evolution
- computed optimal temperature history in the presence of equipment constraints

## Bottlenecks and Open Research Questions

1. How predictive are the models developed by computational chemistry and materials science?  
How predictive will they be in the future?
2. How will nanoscale devices be manufactured in the future? What will the balance be among lithography, stereolithography, nanopositioning, and self-assembly?
3. What will the computer of the future look like?  
CMOS, molecular switches, quantum computing?  
What should we be focusing on?



# Control of droplet-based EWOD/DEP microfluidic systems

T. B. Jones  
University of Rochester

## Goals and Potential Impact if Successful

**OBJECTIVE:** To move beyond accepted fluorophore-based LOC paradigm to "all-electric" molecular detectors for the laboratory-on-a-chip that are based on AC (or DC?) electrochemical impedance diagnostics performed on very small, individual aliquots of analyte and reagent dispensed and transported via EWOD/DEP microfluidics.

**POSSIBLE IMPACT:** A new class of LOC schemes using simple, cheap fabrication technology & having broad application in wet chem/biochem analysis, testing, and processing.

## Approach and/or Accomplishments

### DEP droplet dispensing:

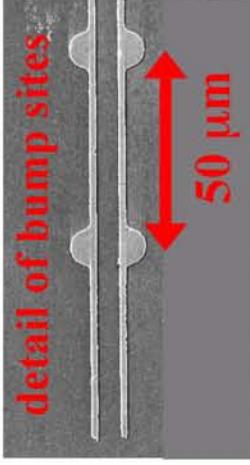
- Controlled dispensing of large number of sessile droplets from ~10 pl to ~100 nl in ~100 milliseconds.
- Aqueous liquids ranging from DI water and ethylene glycol to ~0.1 M phosphate buffer and ~1 M Mannitol.

### Basic investigations of electromechanics:

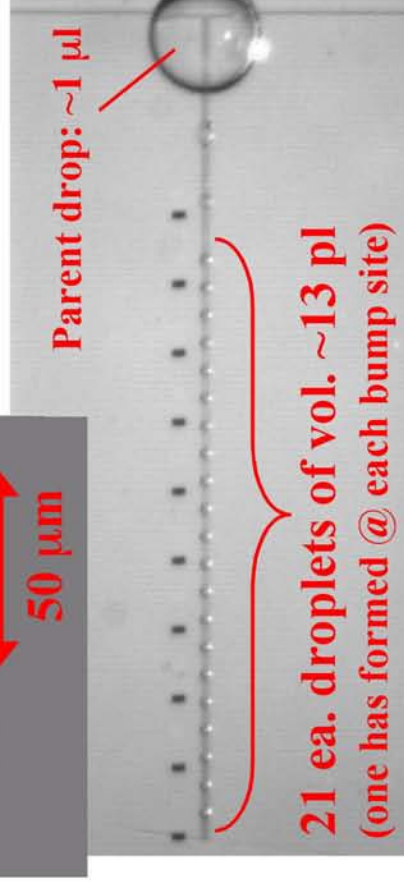
- EWOD & DEP microactuation are, respectively, low- & high-frequency limits of same electromechanical effect.
- Electrically-coupled contact angle effect may influence threshold behavior.

### Feedback-controlled EWOD/DEP microfluidics:

- Test feedback control of high-speed picoliter droplet dispenser based on (i) optical sensing; (ii) voltage modulation; (iii) frequency modulation.



## DEP Droplet Dispenser



## Bottlenecks and Open Research Questions

### Of immediate concern:

- Can we reduce voltage requirement for dispensing sessile droplet of biological liquids with co-planar electrodes to <100 V at 1 kHz. What about DC?
- Can flow sensing and feedback control overcome the variable wetting conditions & wetting hysteresis we now encounter in co-planar structures?

### Larger issues:

- Are "open" versus "closed channel" microfluidic structures complementary or competitive?
- In what applications can we best exploit the speed & geometric simplicity of EWOD & DEP microfluidic schemes?



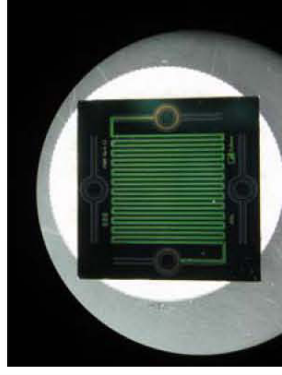
# Modeling of Gas-Driven MicroDevices

## Goals and Potential Impact if Successful

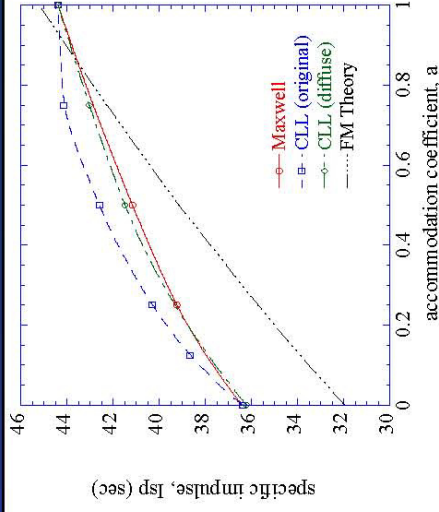
- Enable design and fabrication of efficient microdevices for the control of aerospace vehicles
  - Microsatellites
  - Micro-Air vehicles
- Enable the efficient use of atmospheric sensors
- Understand physical processes of gas-surface interactions that drive microdevice performance
  - Surface area to volume increases significant of surface interactions of gas molecules
  - Current velocity slip models not adequate for some applications
- Kinetic (Molecular) approach required for even relatively high Reynolds number flows

## Approach and/or Accomplishments

- Development of a Direct Simulation Monte Carlo (DSMC) kinetic code for low-speed, gas driven flows in microscale devices
- Use of available gas-surface interaction models for a MEMS fabricated propulsion device have been performed
  - Value of the energy accommodation coefficient is very important in determining device performance
  - Experimental data now becoming available to validate models
- Flows through micro- and nano-porous materials being investigated
  - Atmospheric sensors
  - Phase separators



MEMS fabrication of the Free Molecule Micro-Resistojet (FMMR). FMMR heater chip consists of thin-film metalized heater and gas expansion slots.



FMMR specific impulse versus energy accommodation coefficient for an Argon propellant (DSMC results vs. analytical theory)

## Bottlenecks and Open Research Questions

- Details of gas-surface interactions on micro-engineered surfaces are not known
  - Relatively low speed flows
  - Potential for complex molecules
  - Surface roughness issues
  - Potential for complex surface chemistry and catalysis
- Internal molecular energy accommodation
- Even relatively fundamental data may not be available
  - Energy/Momentum accommodation coefficients
- DSMC builds results based on statistical algorithms
  - Low-speed flows are traditionally noisy
  - Techniques required to obtain meaningful results

# In-Situ Measurement and Control of Nanoscale Synthesis

Pramod P. Khargonekar  
University of Florida

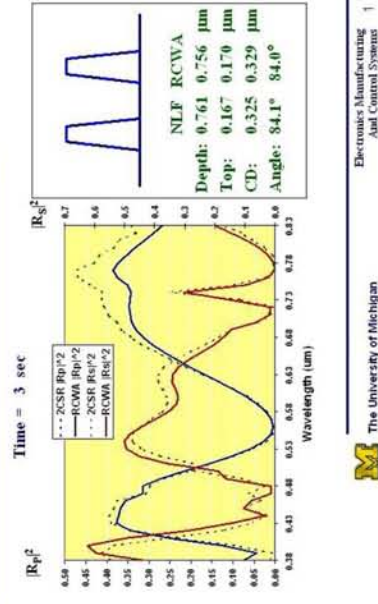
## Goals and Potential Impact if Successful

Physicists, chemists, molecular biologists, and materials scientists have worked on tools and processes to create nanoscale devices. An excellent example is the fabled “writing” of “IBM” by IBM Zurich researchers using a scanning tunneling microscope. We believe that in-situ, real-time sensing and control can make these tools and processes much more powerful in creating designed nanoscale systems. Achieving such in-situ real-time control is a key step in turning these nanoscale processes into “manufacturing” processes.

## Approach and/or Accomplishments

Our approach consists of modeling, nonlinear estimation/filtering, and robust nonlinear control. We have already applied this philosophy and approach to in-situ, real-time sensing and control of plasma etching. This process is widely used in current semiconductor manufacturing technology. Some of our work has been transitioned into industry and has been incorporated into new products.

## Movie



*Doubleclick to play the movie clip*

## Bottlenecks and Open Research Questions

There are several major bottlenecks and open research questions. The first major issue is modeling. How can we obtain computationally tractable models for the physical processes underlying STM, AFM, and other such tools? Here the key is to focus on that part of the physics that is most relevant to the final goal of the process. Next challenge is to develop fast and accurate estimation algorithms to compute reliable and accurate estimates of key state variables. Finally, one will be required to develop control algorithms and implementation schemes to achieve process objectives.



# MEASUREMENT ISSUES AT THE MICRO/NANO SCALES

Jim Liburdy  
Oregon State University

## Goals and Potential Impact if Successful

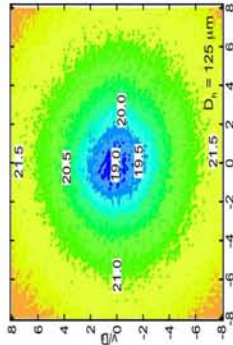
### INSTRUMENTATION

- \*Provide in-situ means to better understand physical processes over extended length scales
- \*Discover limitations and operational characteristics of systems (what are the dominant physical effects?)
- \*Understanding of non-Newtonian physics at nano-scales

### MEASUREMENT

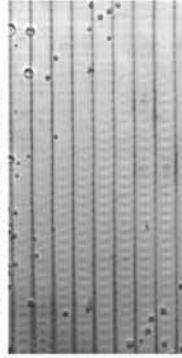
- \*Provide a means to obtain feedback for use in control systems to design complex features and operations
- \*Evaluation of sensitivity of processes to operational conditions – optimization potential

## Micro-Infrared thermal imaging (Narayanan, 2004)



## Microbubble formation/extraction

(Liburdy and Pence, 2003)

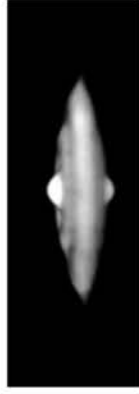


## Fractal branching network (Pence, 2003)



## Surface Instabilities: Droplet formation

(Liburdy and Daniels 2003)



## Approach and/or Accomplishments

- \*New models of sensor form and function (biologically inspired?)
- \*Advances in instrumentation integration with devices and processes (in-situ and noninvasive?)
- \*Ability to obtain global measurements within a system over relevant scales of operation
- \*Development of noninvasive techniques that integrate multiple measurement types simultaneously (velocity, pressure, temperature, concentration, etc.)

## Bottlenecks and Open Research Questions

- \*Noninvasive sensors that can operate over a reasonably wide range of scales
- \*Theoretical basis for operation and detection at very small scales (sensor response when operating in small scale environment – what is the nature of the signal?)
- \*Sensor/system interactions and effects on process being measured
- \*Multiphase flow environments and compatible sensors
- \*Material selection for “harsh” environments (biocompatibility, etc.)

# Nano Mechanical Machining, Manipulation and Measurements

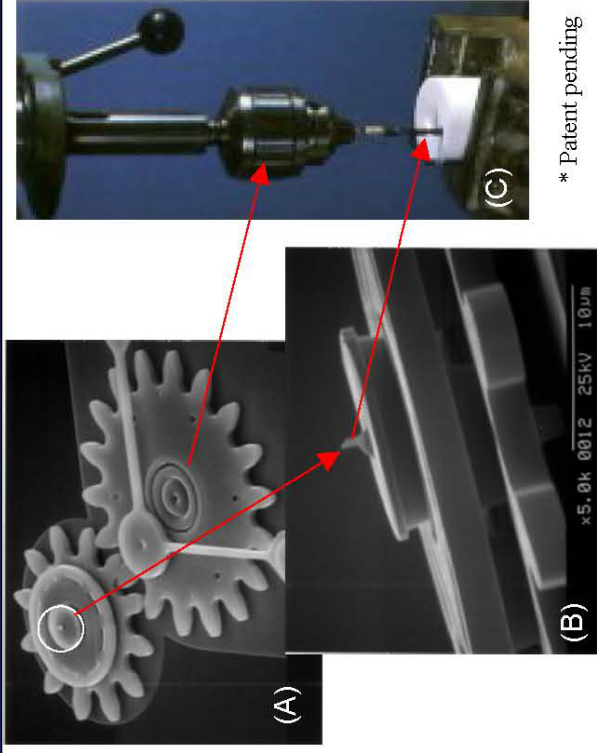
Ajay P. Malshe  
University of Arkansas

## Goals and Potential Impact if Successful

- Design, fabricate and test a nano mechanical machining system on a chip\* (tool, tool holder and their actuation; Graphics A, B), a dynamic scanning probe machining tool, with intention of performing operations such as drilling and milling analogous to its macro counterpart (Graphics C).
- Mechanical machining tools for top-down nano manufacturing of difficult-to-machine materials.
- Pushing application of traditional mechanical machining approach in nano paradigm for directed assembly of heterostructures.
- An excellent testbed to learn materials, mechanism, mechanics and tolerance issues at nanoscale.

## Approach and/or Accomplishments

- Design a micro electro mechanical system (MEMS) based nano machining platform.
- Fabrication of the silicon based nanomachining system-on-a-chip (SOAC) in a batch-fabrication (Graphic A).
- Develop a process to define nanomechanical machining tool (Graphic B).
- Develop scheme for the SOAC installation and demonstrate machining, analogous to macro-machining (Graphic C).
- Successful demonstration of world's smallest nano mechanical machining mechanism.
- Education of engineers in the area of nanomanufacturing.
- Involvement of Junior High School students to create a medium for education of the society.



\* Patent pending

## Bottlenecks and Open Research Questions

- Fabrication of micro system for nano machining and writing
- Fabrication of nano tools and analysis
- Tolerance analysis
- Feed back control system
- Machining and writing process analysis
- Tribological study

*Related References from Malshe's Group- (1) "Mechanical Strength Measurements of Silicon Nano-structures Using Scanning Probe System: An NDE Approach," Journal Smart Materials and Structures, vol. 28, pp. 1028 (2003). (2) "Geometric Error Assessment of a Nanomechanical Drill," Proceedings of IMECE '03, 2003 ASME International Mechanical Engineering Congress & Exposition, Washington, D.C., November 16-21, 2003. (3) "Design Consideration, Process, and Mechanical Modeling, and Tolerance Analysis of MEMS-based Mechanical Machining Systems-on-a-chip (SOAC) for Nanomanufacturing," Proceedings of IMECE 2002, ASME International Mechanical Engineering Congress and Exposition, November 17-22, 2002 New Orleans, Louisiana.*



## Goals and Potential Impact if Successful

- Predict and measure the nonlinear dynamics underpinning
- dynamic stability of straight and coiled carbon nanotubes
- dynamical state transitions in biological macromolecules such as DNA, actin and titin
- periodic & irregular stick-slip motions in atomic and molecular friction
- bifurcations and chaos in scanning force microcantilevers, and nanoresonators

**These are highly nonlinear systems with stochastic inputs**

- Research targets the design of accurate nanoprobe and sensors, better understanding of protein dynamics, and of atomic scale friction for better design of nanoscale systems

## Approach and/or Accomplishments

- Reduced order models of dynamical systems, with strong nonlinearities and possibly non-smooth interactions
- Inclusion of nanoscale van der Waals, Pauli repulsion, electric bilayers, electrostatic forces
- Analytical methods for weakly nonlinear systems have to be discarded in favor of accurate numerical simulations and continuation methods for nonlinear systems
- AFM capabilities enhanced by attaching straight and coiled CNT, & proteins to AFM cantilevers, and their dynamics inferred from that of the microcantilever
- First theoretical and experimental study of nonlinear dynamics of CNT AFM tips in the tapping mode
- Atomic friction and protein dynamics underway

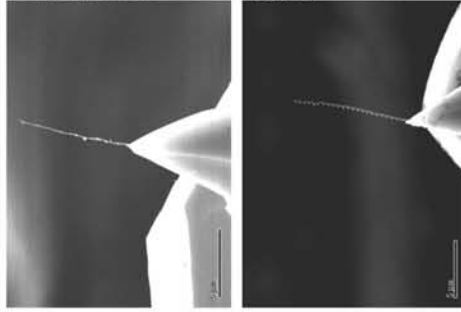


Fig 1. Straight and coiled MWCNT AFM tip. Raman/NASA Ames

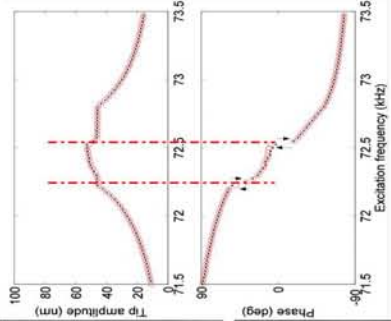


Fig 2. Cantilever amplitude and Phase response while tapping on HOPG. The “bubble” in the amplitude response corresponds to dynamic buckling of the Nanotube (Raman, Reifenger)

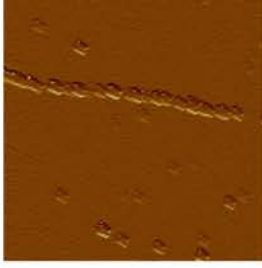


Fig 3. A 2 x 2 μm AFM image of an actin filament Raman/McGough

## Bottlenecks and Open Research Questions

- Dynamics of molecules and CNT's are inferred from microcantilever motions, not determined directly. New instruments need to be developed to monitor the dynamics of these systems
- In matching theory and experiments plenty of parameter uncertainty exist. Nonlinear system identification tools have rarely been used in this arena
- How do CNT instabilities affect AFM imaging?
- What is the atomic origin of friction? Whither thermodynamics?
- How to measure phonon scattering during atomic and molecular scale friction? How to understand dynamical state transitions in proteins?



## GOALS

- Interrogation at the nano-scale with resolution that is orders better than existing schemes
- Interrogation at the nano-scale that has bandwidth that is orders better than existing schemes
- Robust operation so that the need for sophisticated experimental setup is alleviated

## IMPACT

- This will open new regimes of investigation at the nano-scale. Phenomena not observable yet due to high SNR will become accessible to researchers in basic as well as applied sciences
- Very high temporal resolutions will make it possible to study phenomena that evolve rapidly thus opening another front for basic science at the nanoscale.

## APPROACH

- Micro-cantilever based devices form the main tool of investigation
- Use thermal noise constructively to counteract other uncertainties in stabilizing operating conditions. Yield considerably enhanced periods of operation. This results in enhanced resolution
- Use Model based imaging schemes that provide significant advantages in Bandwidth.

## ACCOMPLISHMENTS

- Invented two new methods of imaging:
  - **Transient signal based imaging** (increased bandwidth by 2-3 orders)
  - **Static Non-contact Atomic Force Microscopy** (unparalleled resolution under ambient operating conditions)
- Developed robust control paradigm with Prof. Srinivasa Salapaka for nanopositioning

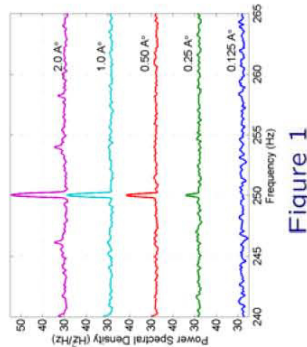


Figure 1

Figure 1: Static Non contact AFM developed by Prof. Salapaka can detect 0.25 Å changes in the sample position *in ambient conditions*.

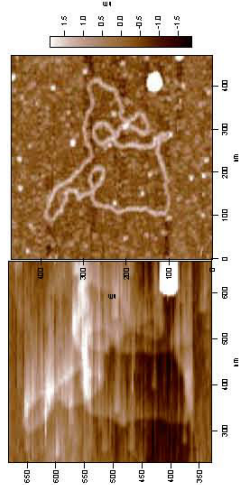


Figure 2

Figure 2: The image (left) is the image of DNA using traditional methods. The image (right) is the image detected by the new model based technique (Transient Signal Imaging).

## Bottlenecks and Open Research Questions

- The quest is for atomic resolution that can be achieved robustly and repeatedly
- The atomic resolution needs to be obtained at relatively high bandwidth
- The main bottleneck is caused by uncertainties and instabilities
- Both are issues where systems and control people can contribute
- Bio-specific imaging schemes is another vital issue
  - Model based imaging can provide these spectroscopy methods.
- Need to disseminate the methods to the application area concerned.



# Modeling optical and bio-optical response of nanosystems

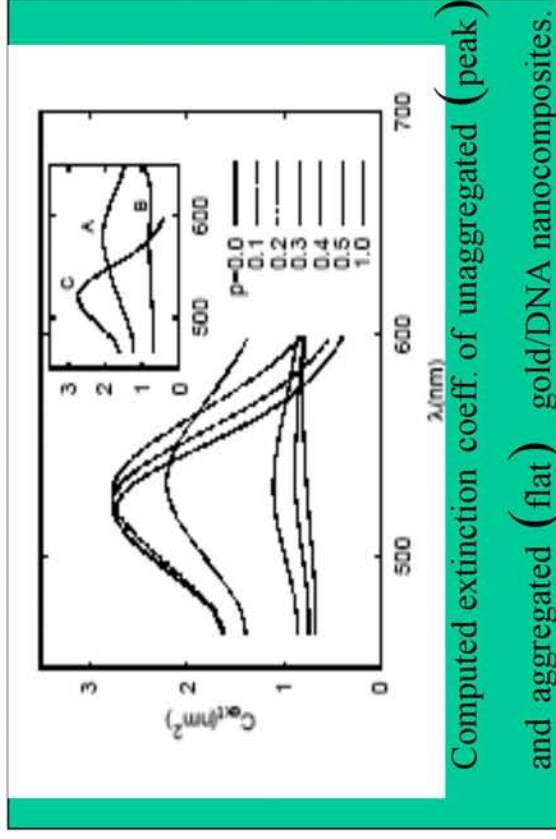
David G. Stroud  
Ohio State Univ.

## Goals and Potential Impact if Successful

1. Successful models will allow control of absorption in metal/DNA nanosystems (and other materials such as small semiconductor particles), using electric fields, structural control, etc.
2. Possibility of exciting new types of materials with tunable optical properties.
3. New ways of producing huge enhancements in selected properties such as second and third harmonic generation.
- 4 May be able to transmit energy in new ways along metal nanoparticle chains.
5. New types of selective sensors for bio-molecules.

## Approach and/or Accomplishments

1. **OPTICS:** Have developed models for optical properties of gold/DNA nanocomposites, including red-shift of peak and broadening on freezing.
2. Developed new ways of calculating surface plasmon dispersion relations along gold nanoparticle chains.
3. Developed models for giant nonlinear optical response of composite materials near surface plasmon resonance.
4. Successfully modeled control of optical properties using liquid crystal coating.
5. **STRUCTURE:** Have successfully modeled melting of gold/DNA nanocomposites, in agreement with expt.



## Bottlenecks and Open Research Questions

How to control and characterize structure? Often, it is difficult to know what the structure of an optical nanosystem is, making modeling difficult.

Modeling techniques are often very computationally intensive. Important to develop new computational and analytical tools.

What are the forces in nano-optical systems? These control structure, but are not very well understood.

Making materials by design: is it possible to produce materials to order with desired optical properties.

Extension of these approaches to other types of properties (magnetic, thermal transport, etc.).



Goal: Develop CAD tools which support MEMS/NEMS use in systems to reduce Design Time from Years to Months

- Must Optimize New Technology in System
  - Do MEMS filters improve RF systems?
- Must Address Nonlinear Model Reduction
  - Trajectory and Statistical methods
- New efforts on design parameterized MOR
  - Enables automatic optimization

## Numerical Model Reduction



- For Linear Problems – Many techniques
  - Krylov-subspace, truncated balance realization, etc
- For Nonlinear Problems
  - Trajectory and Statistical methods
- New efforts on design parameterized ROM

## Approach and/or Accomplishments

- Fast Integral Equation Solvers
  - Faststokes, FastImp, Precorrected-FFT
- Parameterized MOR
  - Extraction of Geometrically parameterized inductors from 3-D E-M solvers
  - Multidimensional Krylov Methods
- Nonlinear MOR
  - Trajectory Piecewise-linear approaches
  - Perturbation TBR analysis

## Bottlenecks and Open Research Questions

- Flexible Fast Coupled Domain Solvers
  - Need to plug-and-play new physics
  - Must handle very complicated 3-D
- Numerical Model Reduction Essential
  - Nonlinear MOR still unreliable
  - Must also include parameterization
  - Massively coupled problems!
- Co-Optimization
  - Parameterized MOR offers new opportunities

# Interfacial Field Velocity Measurements at the Sub-Micron Scale

Minami Yoda  
Georgia Tech

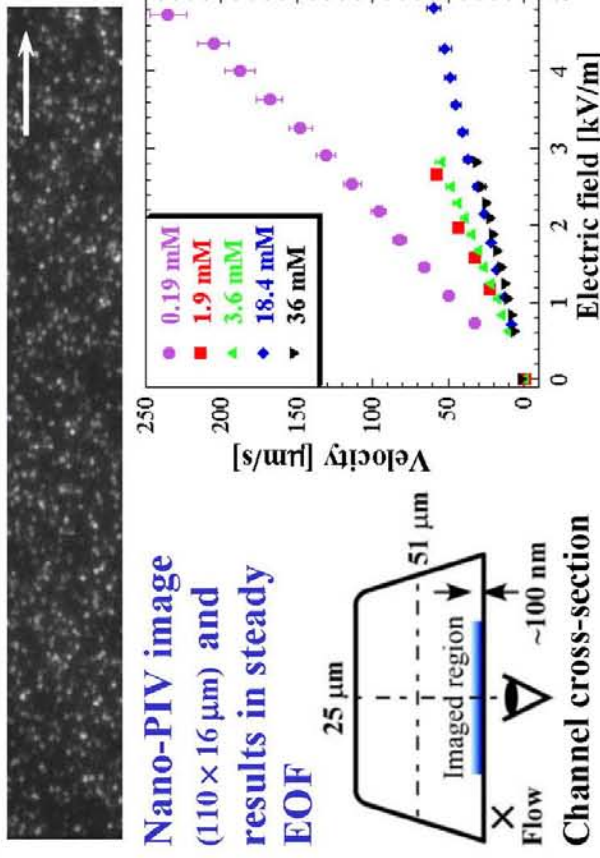
## Goals and Potential Impact if Successful

### Goals:

- Develop robust, accurate and nonintrusive flow measurement techniques at sub-micron/nanoscale
- Develop scaling laws to extend experimental results in microchannels to nanoscale transport
- Study how surface chemistry and roughness affect near-wall transport (*i.e.*, slip)

### Potential Impact:

- Rapid design optimization of micro-/nanoscale devices
- Nonintrusive on-line sensing and control of transport (*e.g.* mixing, throughput) in micro- and nanoscale devices



## Approach and/or Accomplishments

- Developed nano-particle image velocimetry (nPIV): novel technique to measure near-wall velocity fields using fluorescent colloidal particle tracers excited by evanescent-wave illumination
- First velocity measurements in electroosmotic flow in 5–25 μm rectangular channels within 100 nm of wall
- Measured electroosmotic mobilities verified by analytical predictions and independent experimental data
- Evaluated impact of Brownian diffusion on accuracy of nPIV data
- Designing fiber-optic-based source/sensor for evanescent-wave illumination and imaging

## Bottlenecks and Open Research Questions

### Bottlenecks:

- Lack of diagnostic techniques at micro- and nanoscale hampers model development
- From design/fabrication perspective, current models adequately predict “all” measurable quantities
- “Culture” gap between device end users, designers, researchers

### Open Research Questions:

- How do we efficiently control transport in micro-/nanoscale devices?
- What is the new physics (*e.g.* slip, continuum breakdown) in micro-/nanoscale transport?



### ***MEMS Design/Fabrication, Devices, and Systems***

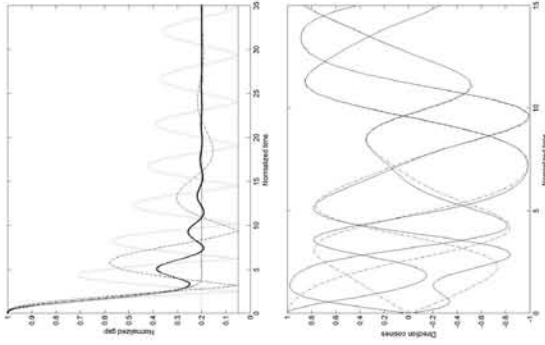
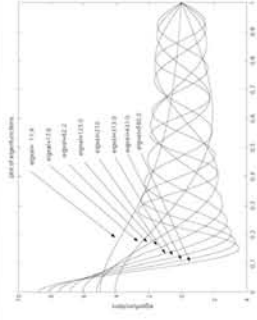
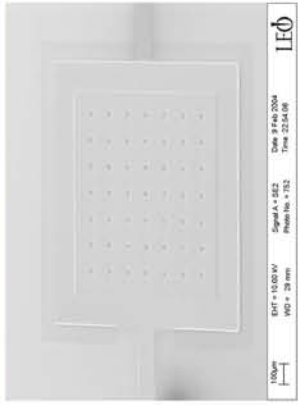
Jordan Berg, Texas Tech University .....	72
Bishnu Gogoi, Motorola Sensor Products Division .....	73
David Horsley, University of California, Davis .....	74
Amit Lal, Cornell University .....	75
Y. C. Lee, University of Colorado .....	76
Woo Lee, Stevens Institute of Technology .....	77
Qiao Lin, Carnegie Mellon University .....	78
Mike Ramsey, Oak Ridge National Laboratory .....	79
Florian Solzbacher, University of Utah .....	80
Darrin Young, Case Western Reserve University .....	81
Babak Ziaie, University of Minnesota .....	82

## Goals and Potential Impact if Successful

- Active control of  $\mu$ mirrors and  $\mu$ mirror arrays for photonics and other micro-optical applications
- Eliminate “pull-in” and “tip-in”
- Reduce overshoot and ringing
- Compensate for fabrication process variation
- Reduce device fabrication costs through smaller capacitive gap, higher yield
- Improve performance with faster switching, more output states, lower control voltages, vibration suppression
- Increase lifetime through decreased electrode contact
- Develop smart adaptive  $\mu$ mirror arrays
- Develop 1 x  $k$  optical switch based on flexible membrane mirror (this work led by W. P. Dayawansa)

## Approach and/or Accomplishments

- Input/output linearization, nonlinear observer design, nonlinear passivity-based control, and energy shaping successfully applied to 1 DOF  $\mu$ mirror model
- Global stabilization of any point in gap, improved transient behavior, reduced control voltage
- Showed importance of velocity estimation
- Constructed intrinsic nonlinear observer for 6 DOF  $\mu$ mirror model using geometric approach
- Output feedback approach generalized to broad class of dynamical systems on Lie groups.
- Stabilize membrane mirror model with output feedback
- Stabilize  $k$  modes of cantilever beam model with two electrodes
- Obtained variety of static and dynamic array patterns with simple local/global interconnection laws (this work led by W. P. Dayawansa)



## Bottlenecks and Open Research Questions

- Hardware issues are critical:
  - Integrated sensors (versus LDV, etc)
  - Control electronics (hybrid MEMS)
  - Parasitic effects (singular perturbations)
- Little penetration of modern control into MEMS community:
  - Cost / benefit not seen as favorable
  - Implementation issues
  - “Circuit-centric”
  - Similar to challenges facing control in other applications areas
- Need for theory / hardware partnerships
- Need for hardware test beds / benchmark problems
- Limited fabrication resources and expertise
- Many challenges in photonic device development based on analog MEMS,  $\mu$ mirror arrays, and flexible membrane mirrors.



# System partitioning considerations for MEMS enabled Microsystems

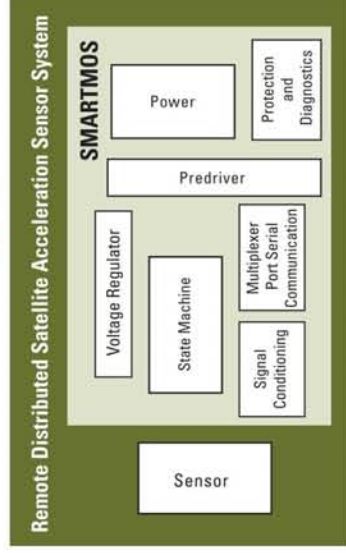
Bishnu Gogoi  
Motorola Sensors

## Goals and Potential Impact if Successful

- Analyze factors that impact Micro-system partitioning - functional and technological level
- Determine figure of merit for the system partitioning model
- Define a comprehensive system model that predicts the performance of the entire system

Enables better understanding of micro-system partitioning challenges, effect of technology choice, application based weighting factors, physical and system model definition, mixed domain system behavior modeling, facilitate efficient micro-system design

Example of a satellite distributed accelerometer system: **Two chips in same package**, circuit considerations had higher weight, needed to be capable of supporting analog circuitry, digital logic, non-volatile memory, high voltage output, high levels of functionality. **Difficult to integrate MEMS sensor with the appropriate CMOS technology**



## Approach and/or Accomplishments

### Classification of key factors

- Identify key factors that influence the partitioning – application, technology, functionality, cost, performance specifications by experience, theory, simple calculations
- Specify parameters for each key factor

### Modeling

- Create some simple model applying mathematical principles using the key factors identified
- Develop a cost function (figure of merit)
- Initiate a common domain for modeling physical and electrical parameters
- Simulate system performance for nominal case and conduct perturbation analysis
- Validate models with test cases

## Bottlenecks and Open Research Questions

**Analysis tools:** Analysis tools for system partitioning definition are not available. A substantial amount of time may be needed to define the appropriate tool for analysis

**Communication gaps:** The development of a system model and suitable partitioning definition requires a suitable communication medium between people from different disciplines or someone who understands a broad spectrum of the technology and functional requirements

**Mixed domain modeling:** It is not clear what is the best software that is suitable for mixed domain modeling and performance analysis. Also, should first principle models be used? Or lumped models be used?

**Test beds for validation:** Selection of suitable test beds for validation of analysis and models



# Optical MEMS for Chemical and Biological Sensing

David Horsley  
University of California, Davis

## Goals and Potential Impact if Successful

Goal: Optically interrogate biological and chemical systems using MEMS devices such as:

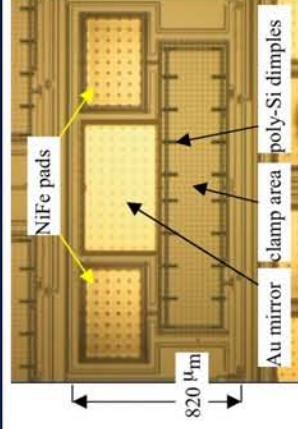
- Infrared spectroscopic chemical sensors
- Optical sensors for particulate measurement in aerosols
- Lab-on-chip devices with integrated optics
- Scanning probe systems

Impact:

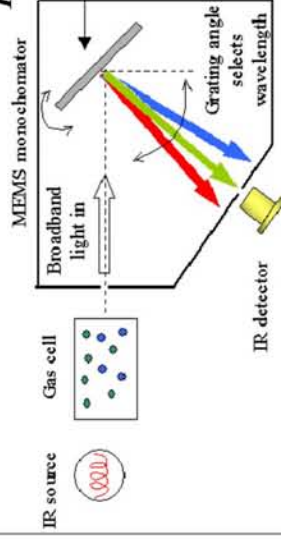
- New tools for measuring nanometer and molecular scale phenomena
- New methods for integrating MEMS and meso-scale components.



Scanning MEMS Mirror



Digital MEMS Mirror



MEMS Monochromator

## Approach and/or Accomplishments

Approach:

- Develop control algorithms and signal processing techniques for an optical-MEMS scanning monochromator.
- Explore application of photonic crystals to optical MEMS devices.
- Investigate magnetic and electrostatic manipulation of particles in lab-on-chip applications.
- Develop control algorithms to accommodate the large parametric variations in MEMS devices.
- Extend optical measurement techniques for device testing and characterization.

## Bottlenecks and Open Research Questions

Modeling: limited tools for modeling photonic crystals and infrared absorption spectra.

- Education: need to train students in materials science, optics, electronics, etc.
- To build systems, we need devices: limited fabrication infrastructure means MEMS researchers often expend effort duplicating the fabrication efforts of past researchers, rather than building off past work to create more sophisticated systems.



# Control of emitted charges from radioactive thin films

Amit Lal  
Cornell University

## Goals and Potential Impact if Successful

- Determine control of emitted radioactive particles at the micro and nanoscale using nanopower low power budget.
- Control emitted energy flow at nanoscale from radioactive thin films could lead to onchip microfluidic pumps and valves that are self-powered – controlled delivery of countable molecules per second for drug delivery
- Microscale RF cavities and permanent magnet fields could be used to create self powered electron guns for nanoscale diagnostics of microsystems
- Tools for microsystem interrogation that do not require “interconnects” and actively modify interfaces – such as biofilm formation on probes

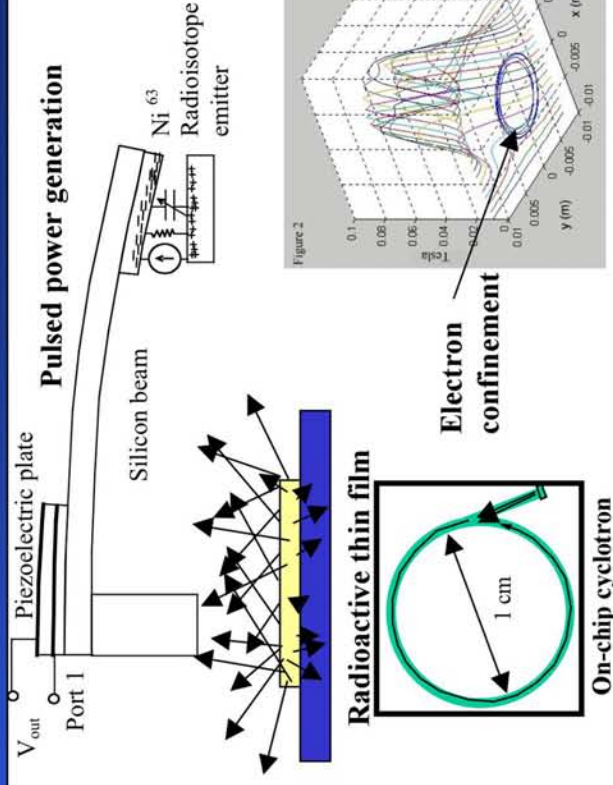
## Approach and/or Accomplishments

We have achieved the following in microsystems:

1. Self-reciprocating mm-cm scale cantilevers powered by radioactive thin films used for power generation
2. Radioactively powered RF pulse generation

Analyze and experimentally confirm ballistic electron transport in:

- A. Nanoscale cascades of solids for coherent electron-hole pair generations
- B. Liquid layers in nanofluidic channels to ionize molecules for fast detection
- C. Gas mixtures to ionize and cause reactions
- D. Nanoscale restructuring of surfaces as electrons are emitted



## Bottlenecks and Open Research Questions

**Science of radioactive thin films has not progressed due to safety issues and perhaps the cold war**

- Electron or alpha particle emission solid angles are not known for thin films – modeling of these effects will lead to an understanding of devices that use monoenergetic particles?
- Safety of thin films: nanoscale packaging of radioactive atoms in scaffolds of non-radioactive elements? MEMS + control
- MEMS microfluidic scale fabrication of radioactive thin films could lead to safe deposition energetic sources?
- Nonlinear phase transitions due to picopower sources?



## Rational Microreactor Design with Nanostructured Catalysts

### Goals (NJ Center for MicroChemical Systems)

Explore microchemical factory concepts for: (1) new chemistry routes with ultra fast heat and mass transfer, (2) just-in-time chemical production via process intensification and miniaturization, and (3) rapid concept to practice via numbering up.

Develop rational microreactor design, fabrication, characterization, and system integration methodologies

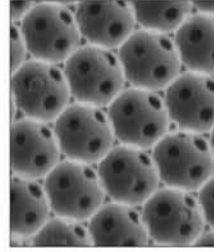
Understand, quantify, and control multi-scale surface phenomena in chemically reacting micro-flow environments.

### Approach and Accomplishments

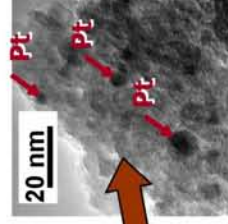
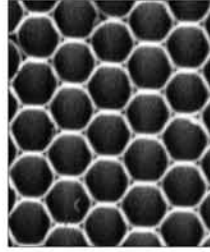
Sequential design, development, modeling and operation of increasingly more complicated microreactor systems.

Portable microreactor systems for  $\text{CH}_3\text{OH}$  steam reforming and CO preferential oxidation through state-of-the-art Si fabrication, kinetic evaluation, and computational tools integration. Stationary microreactor systems for  $\text{H}_2\text{O}_2$  synthesis via direct combination of  $\text{H}_2$  and  $\text{O}_2$  and hydrogenation of pharmaceutical molecules.

Synthesis, immobilization, and integration of nano- and meso-structured catalysts as part of building a library of modular catalyst/reactor platforms.



Self-assembled  
 $\text{SiO}_2$  Support



Selectively infiltrated & immobilized  
2–10 nm Pt particles in amorphous/ $\gamma$   
 $\text{Al}_2\text{O}_3$  support with 2–8 nm pores

### Challenges/Questions

How to develop a generic set of hierarchical design rules for catalyst/reactor platforms in the context of: (1) optimizing reactor system productivity, selectivity, pressure drop, mass transfer, and operational characteristics, (2) minimizing the time required for catalyst material re-formulations without reinventing catalysis, and (3) integrating the latest fabrication innovations?

How to integrate modular catalyst/reactor platforms with “top-down” microchemical factory design criteria from a systems point of view? Can we treat modular catalyst/reactor platforms, as Lego blocks in the toy land of microchemical factories?



# Molecular Biology and Micro/nano-Scale Engineering

Y. C. Lee  
U. of Colorado - Boulder

## Goals and Potential Impact if Successful

Integrate nano-machines, e.g. proteins or their synthetic counterparts, with micro-machines and microelectronic, microwave and photonic devices for novel microsystems having the following potential impacts:

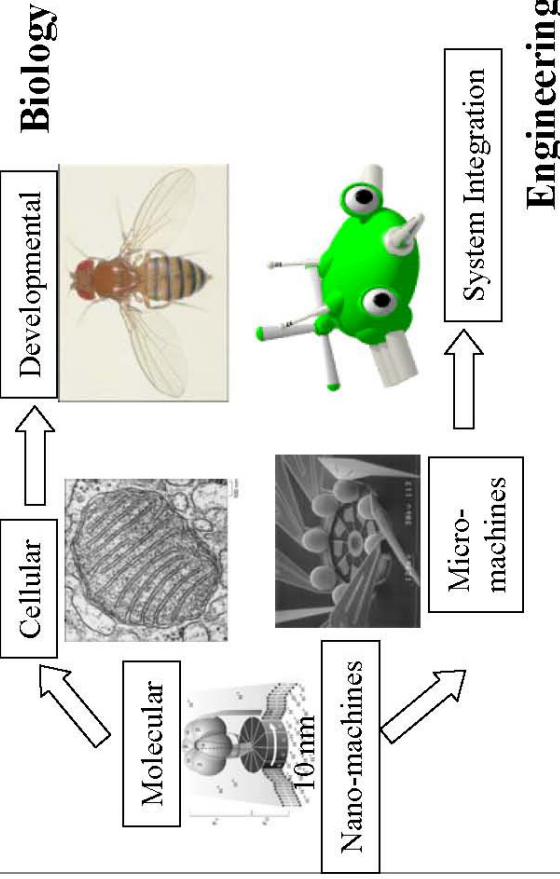
- molecular shuttles for BioMEMS with high-selectivity and high-speed reaction and detection.
- novel sensors and actuators using or emulating biological functions.
- *in vivo* energy sources for *in vivo* medical devices
- alternative energy sources based on sugar, fatty acid or other natural foods.

## Approach

- Identify applications for protein-based, integrated nano/micro-systems.
- Develop packaging and interconnect schemes to integrate nano-machines into micro/nano sub-systems.
- Develop packaging and interconnect schemes to integrate the micro/nano subsystems with other micro-machines to form novel microsystems for the applications identified.

## Accomplishments

- Developed a course for engineering and MCDB students.
- Modified optical and RF MEMS technologies, e.g. atomic layer deposition (ALD)-based self-assembled monolayer, for the self-assembly of nano-machines.
- Developed a feasible concept for a proton engine.



## Bottlenecks and Open Research Questions

- Reliable nano-machines. Most of proteins and their synthetic counterparts are not reliable.
- Reliable micro-machines. Reliable MEMS devices are limited to those without contacts or with point contacts.
- Revised packaging and interconnect hierarchy and corresponding technologies for this new area.
- Surface science studies for reliable self-assembly. There is a need to address assembly yield and reliability.
- Energy conversion from proton gradients into electricity. Bridges connecting nano-machines to micro-machines are needed. One of them is to convert proton gradients generated by nano-machines into electricity to power micro-machines.



# Microfluidic Modeling and Experimentation for Biomolecular Analysis and Characterization

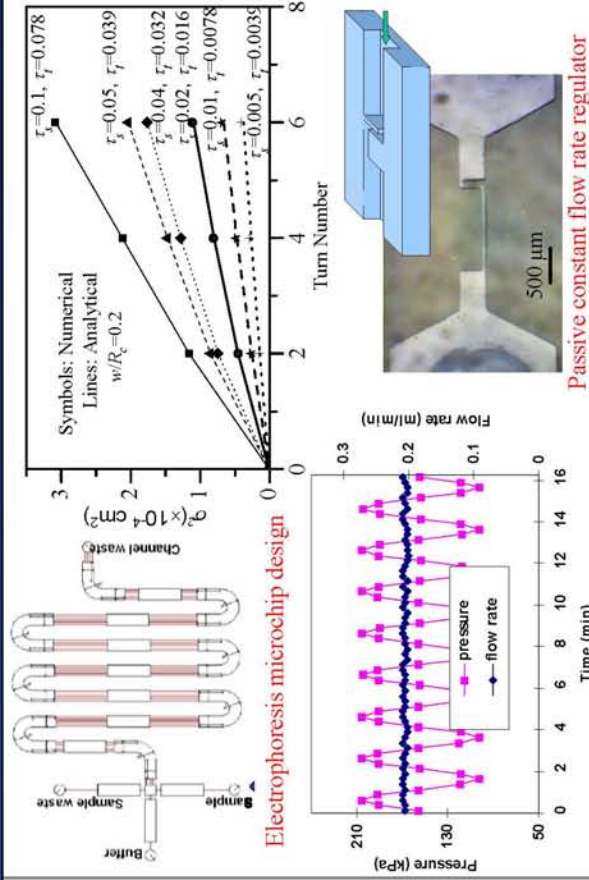
## Goals and Potential Impact if Successful

Science and technology for manipulation & characterization of biomolecules in micro/nanofluidic devices and systems:

- Efficient and accurate microfluidic models appropriate for designing complex systems
  - Innovative liquid manipulation approaches amenable to lab-on-a-chip integration
  - Micro/nanofluidic systems for characterizing fundamental physical properties of biomolecules
- These advances will enable/facilitate fundamental understanding of biomolecules in solution, and result in innovative techniques and design methodologies for integrated, complex miniature bioanalytical devices/systems.**

## Approach and/or Accomplishments

- Develop parametrized, closed-form microfluidic models by focusing on essential physical characteristics, e.g., models for dispersion of electrophoretic separations in complex microchannels due to diffusion, geometry and Joule heating.
- Exploit unique properties of polymers for innovative micro/nanofluidic manipulation. Examples: compliant polymeric microstructures for passive microfluidic control (e.g., valving, flow and pressure regulation); exploring stimuli-responsive polymers in micro/nanochannels for intelligent micro/nanofluidic manipulation and control.
- Employ microfluidics to characterize physical properties of biological macromolecules, e.g. viscoelastic and thermodynamic properties.



## Bottlenecks and Open Research Questions

- Accurate and efficient models suitable for iterative design at both component and system levels as well as for feedback control. These models are desired to be based on first principles, parametrized, and in closed form.
- System integration: technologies for integrating different functionalities on the same chip; especially methodologies for fluid manipulation and sample preparation that are amenable to system integration.
- Biocompatibility: microfluidic/nanofluidic devices need to work not only in well-controlled environments, but in a way compatible with biologically relevant environments (e.g. human/animal tissue).

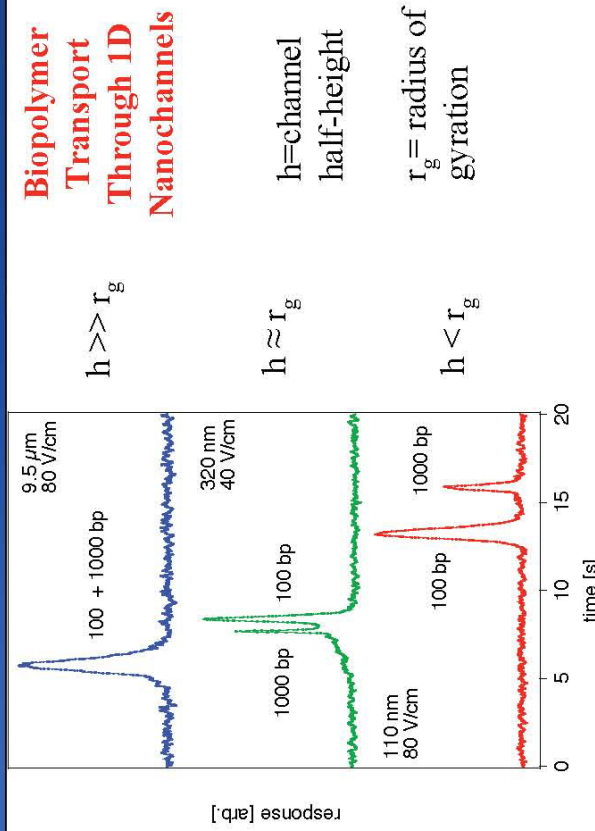


# Transport in Nanoscale Fabricated Fluidic Systems

J. Michael Ramsey  
Oak Ridge National Laboratory

## Goals and Potential Impact if Successful

- Develop understanding of fluid transport in sub-100 nm conduits.
- Develop understanding of macromolecular transport through nanoscale fabricated channels.
- Potential technologies
  - Electrokinetics-based integrated hydraulic pumps for lab-on-a-chip devices
  - Concentration components for sample manipulation
  - Gel free sizing methodologies for biopolymers



## Approach and/or Accomplishments

- Fabrication of 1D and 2D nanochannels using top down methods in glass and silicon substrates
- Observation of fluid and macromolecular transport through single nanochannels under controlled conditions
- Electroosmotic transport observed under electrical double layer overlap conditions
- Size dependent mobilities observed for DNA molecules in nanochannels

## Bottlenecks and Open Research Questions

- Methodologies must be developed to to fabricated channels below 100 nm dimensions
- Tools for interrogating transport at molecular scale must be developed
- MD simulation tools capable of handling short and long length scales

## Goals and Potential Impact if Successful

Operation of MEMS sensors and actuators in harsh environments (temp. up to 650 °C, corrosive gas or fluid environments (e.g. hydraulics fluids, exhaust gas, etc.); temperature and flow control of micro hotplate and microfluidic systems operating in harsh env.

-Micro hotplates for gas analysis systems

-Micro dispenser/inkjet printhead technology (e.g. direct solder printing as replacement for screen printing)

-Lab-on-a-chip / DNA analysis systems

-High temperature pressure/force sensors

**Materials (3C-SiC, GaN, SOI, metallisation systems) and appropriate system design (e.g. wafer/chip level packaging) for harsh environment MEMS**

Improve understanding of material characteristics in harsh env. and modeling of convection and other flow effects on a micro scale to work towards improved simulation tools and better control loop

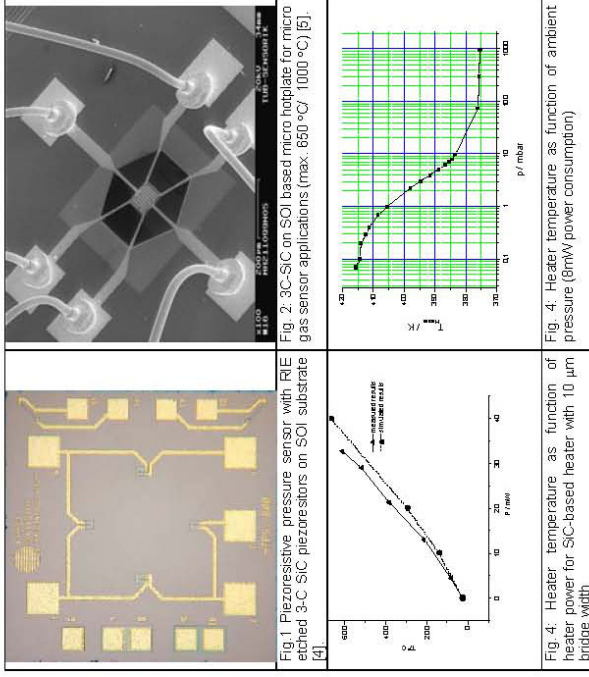
## Approach and/or Accomplishments

Modeling/control:

-studies (analytical and numerical modeling and characterization) on thermal loss effects and convection behavior of micro hotplates  
-improved accuracy of numerical models leading to better device predictability and device control

**Materials/Fabrication technology**

- Study and understand material characteristics changes upon exposure to harsh environments (temperature, corrosive gas atmospheres)  
- Improve long term stability and operation temperature range of chemical and physical devices by use of new Materials (SiC, HfB<sub>2</sub>, SOI, metal oxides)



## Bottlenecks and Open Research Questions

-Reliable modeling and analysis tools (simulation software) is to a large extend unavailable, almost every “task” has to be solved individually using self written software

-Limited understanding of underlying physical/chemical effects leading to uncertainty in model building, particularly when looking at microfluidics / convection effects/surface effects, but also covering understanding of material properties in harsh environments

-Communication between technology/device researchers and application researchers as well as between adjacent fields needs to be improved: we don’t make proper use of a cross sectional technology: MEMS



# Implantable, Intelligent, Wireless Biological Microsystem

Darrin J. Young  
Case Western Reserve University

## Goals and Potential Impact if Successful

### Goal:

- (1) To develop implantable, intelligent, wireless biological  $\mu$ -sensing system
- (2) To develop advanced biological signal processing for identifying new genetic functions
- (3) To develop interdisciplinary research and education

### Potential Impact:

- (1) Innovative biological research methods to gain better understanding of systems biology and new genetic functions discovery
- (2) Revolutionizing health care system and innovative treatment for diseases
- (3) Future interdisciplinary (Engineering/Bio) researchers

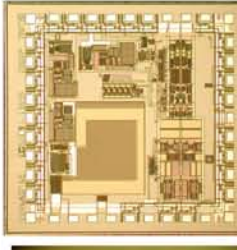
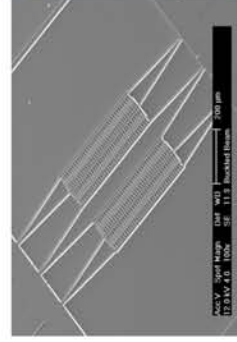
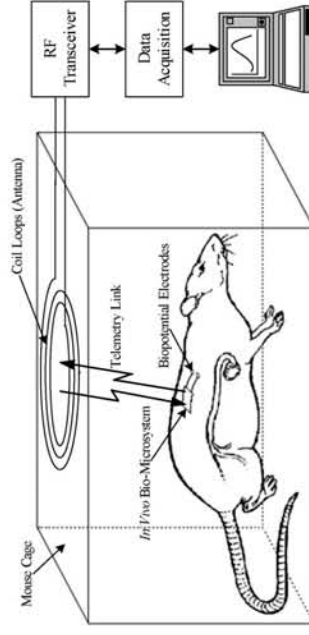
## Approach and/or Accomplishments

### Approach:

- Optimal micro-implant-system architecture
- Miniature micromachined sensors array
- Innovative bio-sensing-packaging technologies
- Advanced bio-signal processing techniques

### Accomplishments

- Innovative minimally-invasive long-term blood pressure monitoring system
- Micromachined strain, pressure, and activity sensors
- Low power CMOS IC for sensor array interface & telemetry



## Bottlenecks and Open Research Questions

- (1) Incompatible micro/nano fabrication technology of sensors (physical, biological, and chemical) and electronics, making it very difficult for system integration and assembly
- (2) In-vivo energy/power sources are limited. Implant-rechargeable battery with RF coils is the only current option, limiting the overall system miniaturization.
- (3) Communication gap between engineering (design and fabrication) and bio/medical people
- (4) How micro/nano fabrication with micro/nano system design can be effectively applied to address critical biological scientific questions?

## Goals and Potential Impact if Successful

To incorporate and/or integrate environmentally sensitive hydrogels with micromachined structures for sensing and smart flow control

Potential impact in the areas of:

- Drug delivery
- Tissue engineering
- Implantable sensors
- Lab-on-a-chip
- Microfluidics

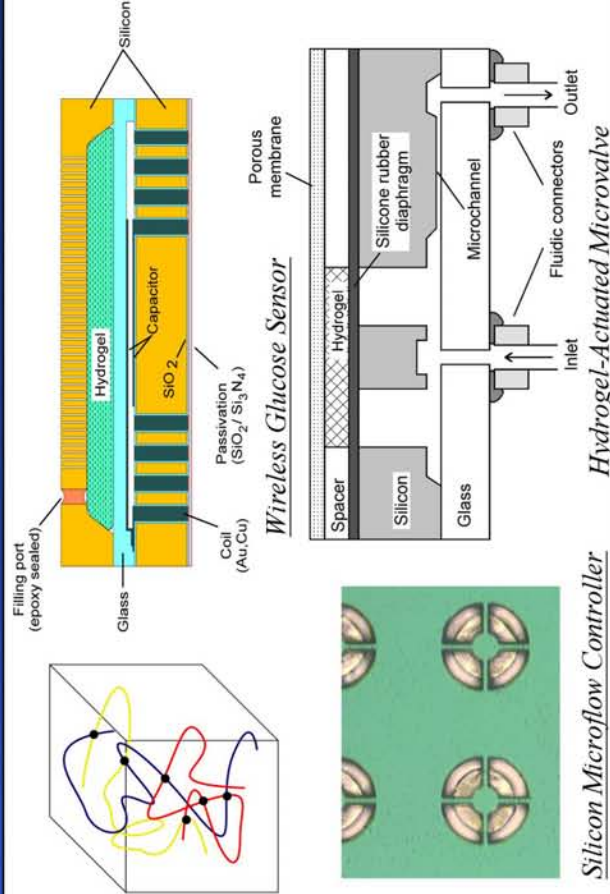
**Hydrogels:** A tangled network of cross-linked polymer chains immersed in a solvent which manifest a reversible and abrupt phase transition in response to a change in an environmental stimuli such as *pH*, *temperature*, *glucose*, etc.

## Approach and/or Accomplishments

We have successfully integrated a variety of hydrogels with MEMS microstructures to fabricate

- Hydrogel-actuated microvalve with porous back-plate
- Glass microflow controller with a cross-cut structure for hydrogel entrapment
- Silicon microflow controller with a double-sided tether structure for hydrogel entrapment
- Hydrogel-based wireless glucose sensor

We have also developed techniques for high-resolution patterning of hydrogel



## Bottlenecks and Open Research Questions

- Batch scale loading in small channels and cavities?
- Adhesion to various substrates?
- Mechanical properties at small scales?
- Surface properties (hydrophobicity/hydrophilicity)
- Process compatibility?
- Functionalization with anti-bodies, DNA, other biomolecules?
- Structural programmability and control?
- Long term reliability?
- Hydrogel-based hybrid material?



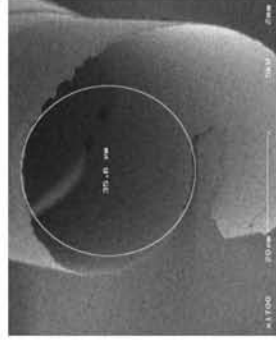
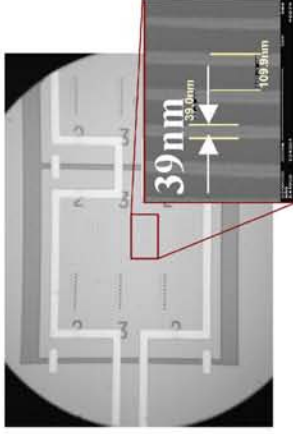
### ***Nanoscale Fabrication***

George Barbastathis, Massachusetts Institute of Technology.....	84
Tianhong Cui, University of Minnesota-Twin Cities.....	85
Jun Jiao, Portland State University .....	86
Nikolai Lebedev, US Naval Research Lab .....	87
Liwei Lin, UC-Berkeley.....	88
Efstathios Meletis, Louisiana State University.....	89
Brad Paden, UC Santa Barbara .....	90
Massood Tabib-Azar, Case Western Reserve University .....	91
Fred Terry, University of Michigan .....	92

## Nanostructured Origami™ 3D Assembly and Fabrication Method

### Goals and Potential Impact if Successful

- 3D Nanofabrication using 2D litho tools
- Hybrid integration of modalities (electrical – optical – mechanical – energy storage, etc.) in micro & nano systems
- Bridge the nanoscale to the macroscale via the 3<sup>rd</sup> dimension
- Create new geometric & topological insights about the use of origami in micro & nanoscale engineering
- Develop the fundamental theory of kinematics, dynamics, and control of 2D→3D folding structures



### Approach and/or Accomplishments

- Use flexible substrates *or* rigid substrates divided into islands hinged together via flexible tethers
- Substrates are *first* nanopatterned and a folding mechanism is developed (e.g. Lorentz force, stress-induced bending)
- *Then* folding mechanism is actuated with specific sequence and timing to result in desired 3D structure
- Demonstrated 2, 3, and 4 layer “paper towel” folds with magnetic and stress-induced actuation
- Solved origami kinematics for arbitrary single-vertex origamis

### Bottlenecks and Open Research Questions

- Alignment and interconnection (presently using templated self-assembly approach) Analogies with and emulation of 3D biological information processing structures (e.g. primate cortex)
- Inverse problem of 2D origami template design from given 3D shape; collision avoidance & integrity
- **in general:** 3D space utilization; connectivity, complexity, information capacity, and adaptivity in sparsely connected 3D micro & nanosystems

Acknowledgments: Henry I. Smith, Stanley M. Jurga, Hyun Jin In, Will Arora // NSF, ARO, DARPA/Sematech



# Nanomanufacturing to Combine “Bottom-up” & “Top-down”

Prof. Tianhong Cui  
University of Minnesota

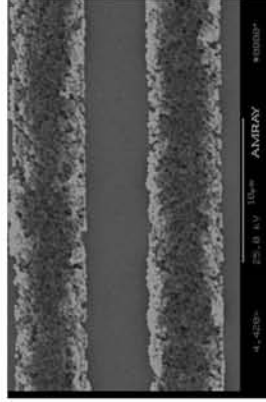
## Goals and Potential Impact if Successful

### Goals:

To fabricate NEMS/nanoelectronics based on the combination of “bottom-up” approaches such as layer-by-layer nano self-assembly and “top-down” techniques such as electron-beam lithography or soft lithography

### Potential Impact:

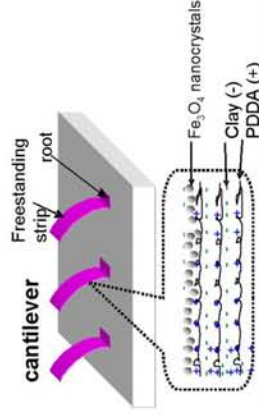
The combination of “bottom-up” and “top-down” techniques will open a new way to realize MEMS/NEMS and micro/nanoelectronics.



Silica nanoparticle thin film patterns



Fluorescent nanoparticle thin film pattern



## Approach and/or Accomplishments

### Approaches:

- Modified lift-off
- Metal mask

### Accomplishments:

- The above approaches based on nano-assembly and UV lithography have been investigated.
- Nanoparticle-based MEMS (magnetic cantilever beams) and microelectronics devices (capacitors and field-effect transistors) have been fabricated and characterized.

## Bottlenecks and Open Research Questions

My lab is currently spending the majority of its time on the combination of layer-by-layer nano assembly and electron-beam lithography/soft lithography.

- What is the optimum processing conditions for the nanomanufacturing?
- How to well control the processing to realize condense and uniform nanoparticle patterns?
- How to realize the NEMS and nanoelectronics devices and systems with few defects?

### Goals and Potential Impact if Successful

- Develop novel techniques for controlled fabrication of triode-type nanotube and nanowire field emitter arrays
- Reduce the required voltage, enable the modulation of the emission current, and provide more control for small arrays such as the pixels in flat panel displays.
- Create new field emission sources with improved gate voltage, long lifetimes, and high stability of emission current in comparison to those of conventional metal and silicon field emitters.
- Promote the potential applications in high frequency amplifiers, high frequency traveling wave tubes, flat panel displays, multiple electron beam lithography, and portable x-ray sources.

### Approach and/or Accomplishments

#### Nanofabrication:

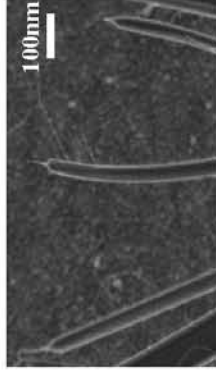
- Optimize synthesis conditions for high quality nanotubes and nanowires
- Fabricate micro-gated nanotube and nanowire emitter arrays of various configurations using combined FIB and CVD technique
- Explore procedures for the scaling issues

#### Electrical Property Characterizations:

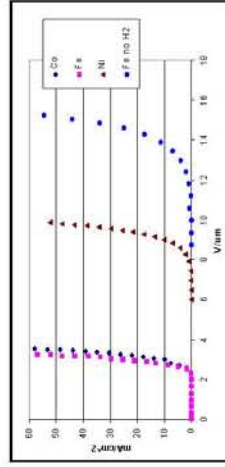
- Evaluate the field emission behavior of the emitter arrays
- Measure the gate to cathode capacitance
- Investigate the interface effects between the nanotubes, nanowires and the substrate



Nanowire arrays fabricated by FIB



SiO<sub>2</sub> nanowire emitters



Controlled growth of nanotubes in column structure

I-V characteristics of nanotubes synthesized from different catalysts

### Bottlenecks and Open Research Questions

- There exists a lack of reliable techniques for controlled growth of nanotubes and nanowires
- Existing techniques for fabricating nanodevices are inadequate for reliable mass production of nanotube- and nanowire-related devices
- When fundamental nanomaterials science problems are still critical, nanodevice fabrication is even more difficult
- How to establish a strong tie among the materials scientists, theoreticians, and device engineers to ensure the realization of the nanodevice technology?



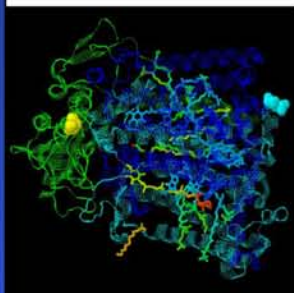
# Local Energy Sources for Bio-Inorganic Devices

Nikolai Lebedev  
Naval Research Laboratory

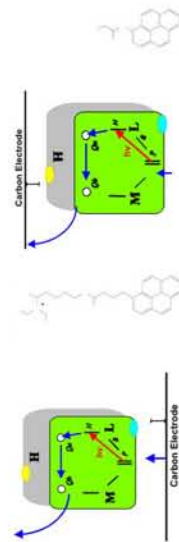
## Goals and Potential Impact if Successful

System integration at nanoscale level requires specific energy supply and information reception. Spatial and temporal regulation of these functions can be used for the control of the device assembly.

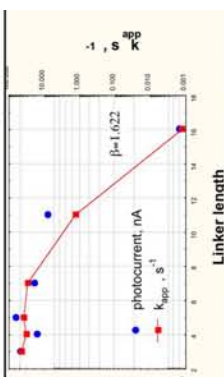
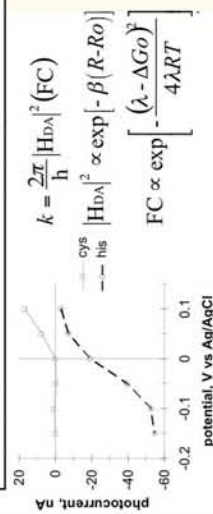
Incorporation of photosynthetic proteins into bioinorganic devices allows for construction of ultra light high power density local energy sources, ultrafast low light imaging photosensors and integrated nanoelectronic devices for information processing.



Two ways of oriented binding of photosynthetic reaction center (RC) to electrode:



Optical gating, rectifying effect and control of the efficiency and direction of electron transfer at electrode by RC orientation, distance and driving force:



## Approach and/or Accomplishments

Recently we have developed a new approach for protein oriented binding and demonstrated orientation dependent photoinduced electron transfer and generation of local electric fields at bio-inorganic interfaces. Our approach is rather universal and can be integrated and used for regulation of the performance and assembly of various nanodevices. We have tested it for carbon nanotubes, nanoporous oxide electrodes, flat conductive surfaces like gold and ITO, lipid membranes and ion channels.

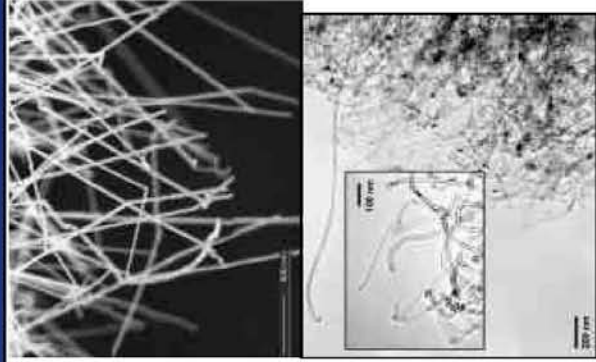
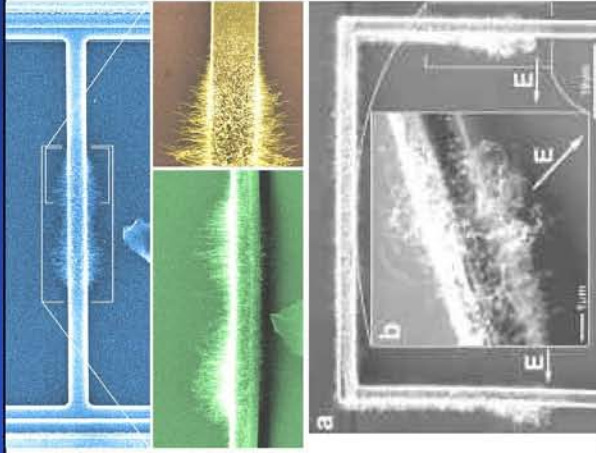
## Bottlenecks and Open Research Questions

The main rate limiting step in energy and information transfer in bio-inorganic devices is electrical connection at the interfaces. This can be improved by striping insulating parts from the proteins using molecular biological approaches, design and chemical and biological synthesis of specific conductive linkers. Development of new experimental tools for multiconnection wiring of biological molecules would be also of great importance.

## Synthesis, Assembly and Integration for Nanowires/Nanotubes

### Goals and Potential Impact if Successful

- We are developing post-CMOS processes for direct synthesis, assembly and integration of nanowires/nanotubes for sensing, actuation and communication applications
- The goal is to use foundry services for circuitry and post processing for nanostructures for low manufacturing cost
- This opens up the integration of bottom-up and top-down processes taking advantage of both approaches
- No post-assembly process is required for nanostructures by using self-synthesis, self-assembly and self-integration



### Approach and/or Accomplishments

- Localized heating and synthesis of nanostructures using the VLS growth mechanism with localized heating
- Proof-of-concept demonstration on the synthesis of nanowires and nanotubes of 5~80 nm in diameter and up to 10 μm in length on a MEMS bridge
- Proof-of-concept demonstration of self-assembly of nanowires and nanotubes between two MEMS bridges
- Preliminary demonstration of gas sensing of assembled nanotubes

### Bottlenecks and Open Research Questions

- Control of the synthesis process including diameter, orientation and properties of nanowires/nanotubes
- Doping of silicon nanowires
- Electrical contact properties of nanostructures
- Packaging
- Circuit integration
- False readout



# Self-assembled Nanostructures in Thin Films

Efstathios Meletis  
Louisiana State University

## Goals and Potential Impact if Successful

Control self-assembly of oxide and metallic nanostructures through fundamental understanding for:

- nanofabrication and nano-imprinting
- nanopatterning and templating
- nanoelectronic devices, nanosensors, memory devices, etc.

Development of a novel 'bottom-up' method to design and manufacture nanodevices.

Require fundamental understanding of the self-assembling mechanism through innovating experimentation coupled with atomistic modeling and simulation to capture the nanoscale physical phenomena involved.  
Integrating nanostructures in devices.

## Approach and/or Accomplishments

### EXPERIMENTAL:

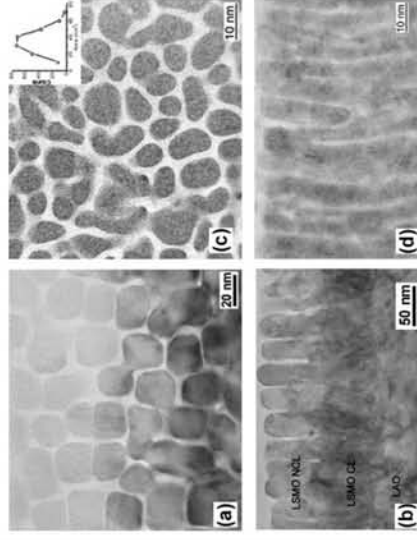
Device and design appropriate experiments to explore and understand the role of processing and material parameters on the resulting self-assembled nanostructures.

### MODELING:

Use combined atomistic (molecular dynamics and kinetic Monte Carlo) and mesoscale simulations to model nanostructure growth and extend the model to design future systems of interest.

### ACCOMPLISHMENTS:

Self-assembled nanorods have been achieved in Co/DLC nanocomposite and  $\text{La}_{0.8}\text{Sr}_{0.2}\text{MnO}_3/\text{LaAlO}_3$  epitaxial films.



(a), (c) Plan-view TEM and (b), (d) XTEM of  $\text{La}_{0.8}\text{Sr}_{0.2}\text{MnO}_3/\text{LAO}$  and Co/DLC nanostructured film. **Ordered nanorods** formed by (a) direct deposition on a substrate or (b) nano seed fabrication.

## Bottlenecks and Open Research Questions

- **Appropriate processing techniques** that can capture and control range of parameters dominating the self-assembling process are needed. This applies to both, ceramic and metallic nanostructures.
- **Better coordination between experimental and theoretical studies.**
- **Multiscale modeling and simulation methods** are needed to better handle the time and length scales involved.
- **Lack of appropriate methods** for integrating the self-assembled nanostructures into nano/micro devices.

# Nanofabrication of materials by self-assembly

## Goals

- Coat surfaces with dense uniform self assembled monolayer using two synthetic routes: **organic solvent & supercritical CO<sub>2</sub>**
- Observable macroscopic properties due to monolayer

**We are creating inorganic/organic materials with a nano-interface and functionality.**

## Applications

### I. Composite Materials

Enhancement of strength, toughness

Adhesion, release

### II. Antimicrobials

Medical devices (catheters, implants, etc.)

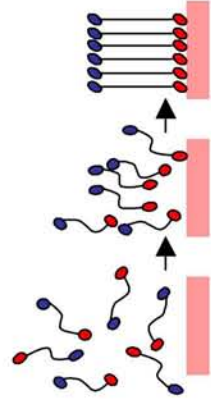
Medical sensors

### III. Chemical Sensors

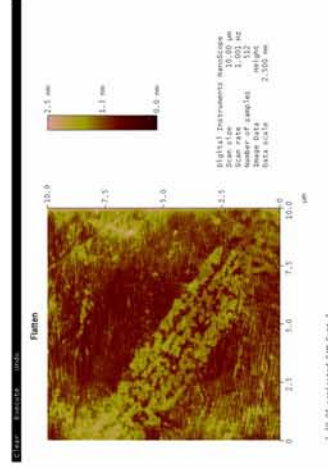
Medical Diagnostics

Molecular detectors

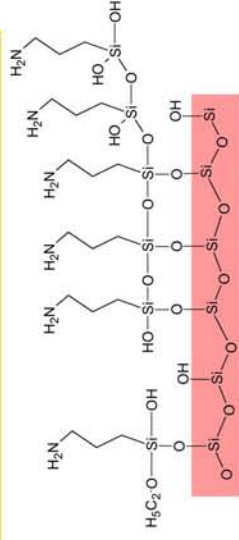
### IV. Filter media



**Thermodynamic self assembly on surface**



**AFM coated Si Wafer**



**Covalent bonds**

**Surface-silane, silane-silane**



**Diatoms (100's nm each)**

## Approach

### Control

Temperature and pressure in the SCCO<sub>2</sub> system will affect solubility, reaction dynamics and material losses

Material hydration for surface reaction

Silane concentration

Fluid mixing for diffusion of reactants

### Modeling

Equilibrium phase behavior of reactants to maximize solubility

Reaction kinetics of silanization (T, P, conc.)

## Problems and future concerns

- Obtaining uniform coverage and maximum cross-linking between surface silanes
- Characterization methods: AFM and solid-state NMR
- Coating materials which are inert (carbon fiber) without degrading the materials properties.
- Characterizing macroscopic improvements resulting from nanometer sized additions
- We are far from what nature can already do - diatoms form spontaneously at room temperature and are very strong and porous.

*Collaboration w/ Jennifer Politsch, ISC*



# Nanometrology and Bottom-Up Nano-Devices

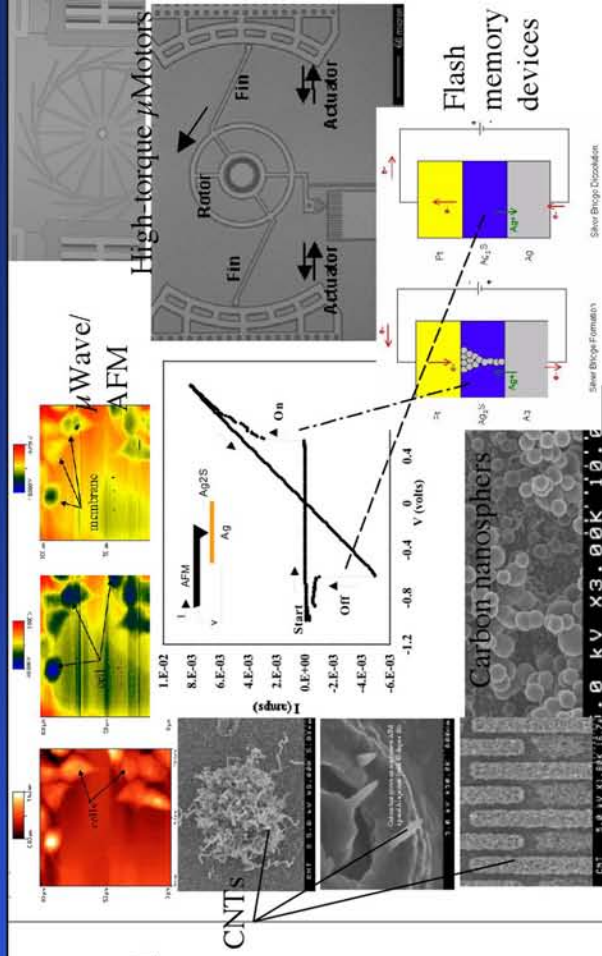
Massood Tabib-Azar  
Case Western Reserve University

## Goals and Potential Impact if Successful

- Electromagnetic (1-100 GHz) imaging of embedded nano-structures with atomic resolution in electronic and biological materials to understand their interactions and properties.
- Development of bottom-up techniques to enable integration of nano-scale devices and “objects” with lithographically defined submicron-scale structures.
- Development of flash memory devices based on solid-electro chemical cells and programmable nanowires
- MEMS actuators capable of producing large force/displacement with small excitation voltages/currents
- Novel microactuators for bio-medical and micro-fluidic applications

## Approach and/or Accomplishments

- We have added microwave measurement capabilities to atomic force microscopy to simultaneously scan topography and permittivity/conductivity of inorganic/organic and biological samples over 1-20 GHz. Embedded nano-structures are thus imaged in these materials.
- We have developed CuS/Cu-based solid electrochemical cells and have shown that nanowires can be reversibly grown and etched by passing current through them. These devices may form the basis of post 2010 flash memory devices.
- We have designed and fabricated micromotors that operate by mechanically rectifying oscillatory motion to achieve very high torque and scalability over a wide range ( $\mu\text{m-cm}$ ).
- We are adding carbon nano tubes and nano spheres to MEMS structures to fabricate GHz oscillators and mass spectrometers



## Bottlenecks and Open Research Questions

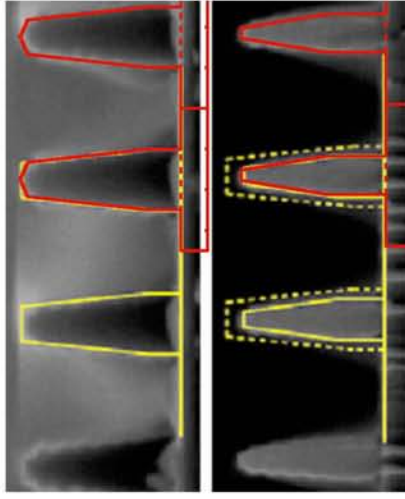
- Materials and their processing still remain one of the most important bottle-necks in device development. The fabrication process also pause some very challenging problems that need to be addressed to truly take advantage of bottom-up devices.
- Direct imaging and characterization tools with the ability to “see” interfaces in nanometer-scale and quantitatively measure their properties need to be more fully developed.
- Methodologies to deposit/process and characterize many different materials simultaneously and in parallel also should be developed for material/processing discovery



### Goals and Potential Impact if Successful

- Real-Time, in situ monitoring of the evolution of topography on the sub-micron and nanoscale during both top-down and bottom-up fabrication process
- **Real-Time feedback & feedforward control of micro/nanofab processes for high precision manufacturing**
- Improved understanding of chemistry and physics of fabrication processes
- Potential applications of optical remote sensing for non-semiconductor problems (biological/chemical)
- Sensing and feedback control are needed for evolutionary improvements in current top-down manufacturing and should prove valuable in new nanofabrication processes

- 350nm Photoresist Lines on SiO<sub>2</sub>/Si Before Trim-back + Overlay Profiles Extracted with Nondestructive in situ Optical Measurement (top figure)
- Similar Photoresist lines reactively ion etch to a bottom dimension of 200nm under automated control



Start: CD 296.7±9.1nm

Trimmed: CD 189.1±29.3nm

### Approach and/or Accomplishments

- Monitoring: Some of the 1<sup>st</sup> demonstrations of critical dimension/topography extraction from gratings using spectroscopic ellipsometry and reflectometry
- The 1<sup>st</sup> real-time, in situ “movies” of topography evolution in reactive ion etch systems
  - Also developed a unique RF plasma spectroscopy tool
- Control: The 1<sup>st</sup> and only examples of real-time endpoint detection based on critical dimensions – etching to target CD
- A factor of 3 improvement in etch depth reproducibility using SISO control of plasma density on an industrially standard process and improved the physiochemical understanding of the dynamics of the Cl<sub>2</sub>/Si etch process

### Bottlenecks and Open Research Questions

- Optical topography extraction methods work to sub-100nm scales but are becoming challenged due to wavelength limitations – development of instruments in the EUV range is needed
- Experimental data on the optical properties of materials in nanometer regime is limited at best
- Optical topography extraction for non-period structures has barely been explored due to both computational and measurement problems. This limits current industrial use and possible uses in the nano regime.
- Applications of real-time control in micro-scale manufacturing are limited due to sensing and detailed process understanding issues



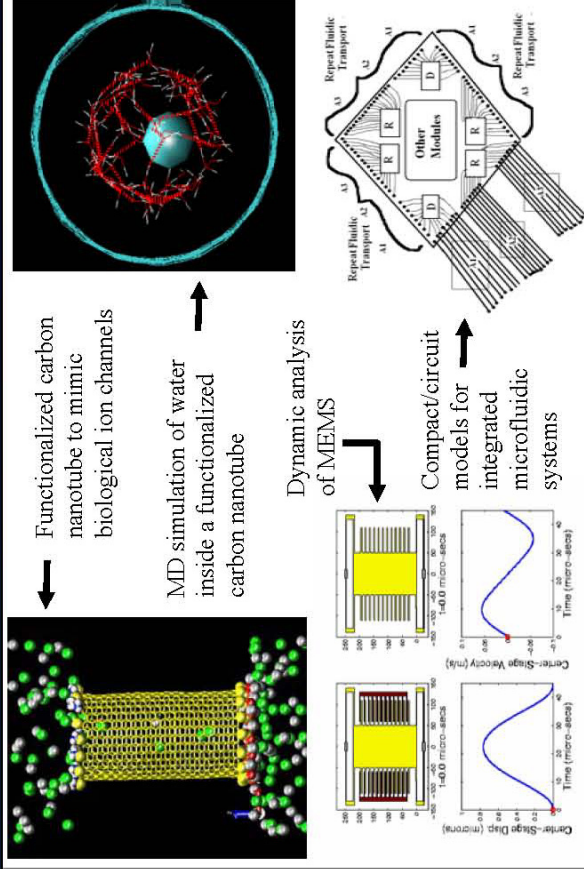
## ***Miscellaneous***

Narayan Aluru, University of Illinois at Urbana-Champaign .....	94
Rod Beresford, Brown University .....	95
Daniel Burns, Air Force Research Laboratory.....	96
Cetin Cetinkaya, Clarkson University.....	97
Tim Dallas, Texas Tech University.....	98
Gary Fedder, Carnegie Mellon University .....	99
Albert Henning, Redwood Microsystems, Inc.....	100
Peter Hesketh, Georgia Institute of Technology .....	101
Roberto Horowitz, UC Berkeley .....	102
Chang-Soo Kim, University of Missouri-Rolla .....	103
Martin Schmidt, MIT .....	104
Sharon Smith, Lockheed Martin Corporation .....	105
Shankar Sundaram, CFD Research Corporation .....	106
Marvin White, Lehigh University .....	107

## Goals and Potential Impact if Successful

- Develop fast and efficient design tools for mixed-domain analysis of microelectromechanical systems (MEMS)
- Develop physical models and computational tools for analysis of nanoelectromechanical systems (NEMS)
- Develop a fundamental understanding, physical models and multiscale simulation tools for liquid and gas flows through nanometer scale channels

The availability of accurate, efficient and robust design tools will enable rapid computational prototyping of complex and novel mixed-technology systems for various applications



## Approach and/or Accomplishments

- Full Lagrangian and meshless techniques for efficient mixed-domain analysis of MEMS (mechanical, electrical and fluidic)
- Classical, semiclassical and quantum-mechanical models for analysis of NEMS
- Reduced-order and compact models for circuit-level analysis of integrated MEMS and microfluidic systems
- Atomistic, continuum and multiscale simulation tools for analysis of liquid flows in nanometer channels
- Identification of new physical phenomena (e.g. flow reversal) in nanopores
- Development of synthetic ion channels to mimic biological ion channels

## Bottlenecks and Open Research Questions

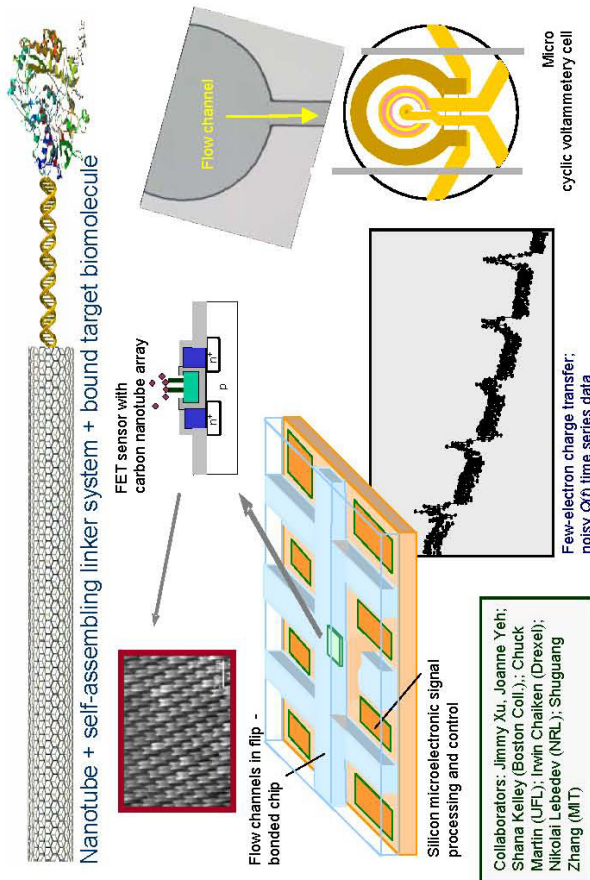
- Development of efficient and accurate multiscale tools combining quantum-mechanical, atomistic, mesoscale and continuum approaches is challenging
- Lack of models for all the new physical phenomena encountered in nanotechnology
- Lack of proper experimental data (especially in nanotechnology) to validate simulation tools and physical models
- Automatic reduced-order models, complex 3D geometries, material properties, metrology, inter-atomic potentials, algorithms, uncertainty quantification, stochastic models, integrated system analysis, .....



# Nanoelectronic Sensing and Control of Biomolecular Events

## Goals and Potential Impact if Successful

- Scalable protein-specific self-assembly of biomolecules to nanoelectrode arrays
- Reliable and efficient electron transfer between biomolecules and digital electronic readout
- Multiple-molecule real-time *in situ* detection of hazards and metabolic status
- Ultimately, closed-loop sensing and control of biomolecule concentrations *in vivo*



## Approach and/or Accomplishments

- Target molecules are redox-active, or can trigger redox activity on binding
- Molecular linkers to recognize target, tether to a nanoelectrode array, and conduct electrons
- Functionalized nanoelectrodes, such as carbon nanotube, synthesized on field-effect transistor gate layer
- Integration of microelectronic signal processing and microfluidic analyte manipulation
- Design of extremely low-level charge and current sense amplifiers

## Bottlenecks and Open Research Questions

- Molecule-specific self-assembling for many proteins
- Stability/affinity (mechanical, biochemical, electrochemical...)
- Scaling up (in protein types) and (down in protein numbers)
- Nanoscale electrode fabrication; wiring to nanoelectrodes
- Quantum efficiency of electron capture and transport
- “Single protein” detection at 300 K
- Stochastic signal processing and information extraction





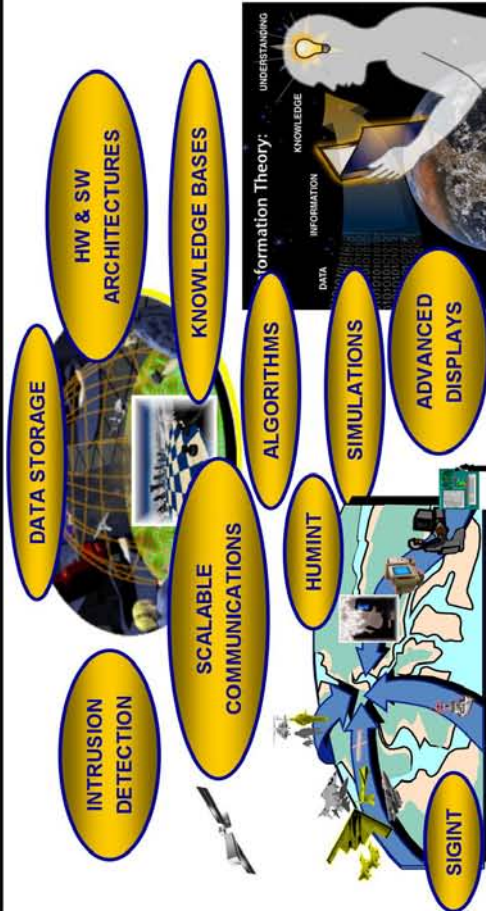


# Nanotechnology (IF Directorate Interest Areas Only)

## Novel Information Processing Paradigms Thrust



Objective: Exploit Properties of Nanotechnology to Revolutionize Information Dominance.



### Approach

- Creation of Integrated Systems through Control of Matter on the Nanometer Length Scale
- Design Tools for Nano-Bio-Info Systems
- Simulation, Analysis & Characterization of Atomically Controlled Materials and Structures
- Exploitation of the Electronic, Optical, Magnetic, Chemical, Biological and Mechanical Phenomena and Properties Dominant at <100 nm Scale
- Investigate and Develop Algorithms for Nanotech Architectures

### Impact

- Revolutionary Computing Architectures for Information Dominance
- Decision Aides Approaching Human Intelligence
- Distributed, Interactive C2 Simulation and Visualization
- Distributed and Networked Sensing, Fast, Sensitive Chem/Bio-Threat Detection
- Autonomous Space Operations, Dynamic Stealth

### Status – TRL2

- DARPA Biocomp/Simbiosys/Cogn programs now
- THz IR detector, Picosat, NMEMS RF, Quist, CITE)
- Approved 06 POM line for AFRL TD WG program:
  - advanced materials, electronics, energetics
  - M&S, design integration, self-assembly X-cuts
- IF summer projects: 3D nano-architectures, bio-sensor design opt. (2/ bio-like genetic algorithms)
- Coordinations: OSD review, NSF/DARPA workshops on self assembly, M&S & integration
- In-house projects for Emerg. Tech. M&S, design tools
- Would like to do fast simulation platforms for intuitive and evolutionary design methods

POC: Daniel Burns, 315-330-2335, Email: [Daniel.Burns@rl.af.mil](mailto:Daniel.Burns@rl.af.mil)

1 October 2002



# Motion/Adhesion/Removal of Micro/Nano-Particles on Surfaces

Cetin Cetinkaya  
Clarkson University

## Goals and Potential Impact if Successful

*Main Objective :* To develop a manipulation and transport system for integrating existing micro/nano-scale building blocks to construct nano/micro-scale structures and systems. To achieve this goal, the following tasks are carried out:

- + Excitation and control of motion of micro-particles on dry surfaces (see Figs. 1 and 2 for motion of a four-particle pack and guided motion of a particle in a trench, respectively),
- + Development of non-contact work-of-adhesion measurement systems for small-scale objects, and
- + Development of removal techniques for nano-particles.

*Potential Impact:* Development of flexible nanomanufacturing tools.

## Approach and/or Accomplishments

*Approach:* Utilize high-frequency bulk and surface acoustic waves for exciting motion of micro-particles on dry surfaces. The choice of the use of acoustics waves and adhesive forces as driving forces for manipulating micro/nano-objects and joining them together lies in a fundamental length scale argument.

*Accomplishments:*

- + We have accomplished generating linear and rotational motion of micro-particles on silicon surfaces using MHz-level bulk elastic waves.
- + We have, for the first time, demonstrated that PSL particles as small as 60nm from silicon wafers can be removed by using plasma-induced shock waves.

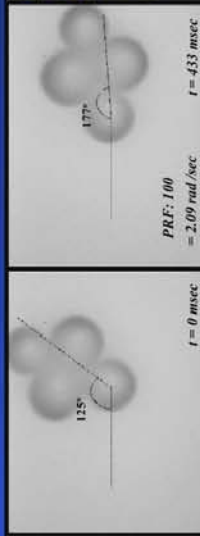


Fig. 1 The rotational motion of a four-particle pack of 20µm latex particle on silicon under base excitation (Left).

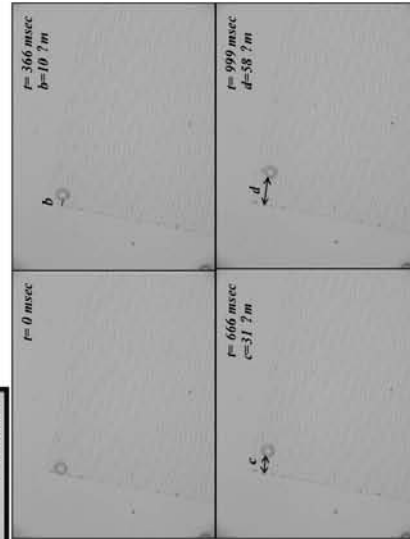


Fig. 2 The guided motion of a 20µm-latex particle in 10µm-trench under MHz-level axial base excitation (Right).

## Bottlenecks and Open Research Questions

- + Manipulation, handling and removal of micro/nano-scale objects is a challenging bottleneck problem in many nanomanufacturing and nanotechnology applications.
- + Present focus is on the development of (mathematical and experimental) techniques for the accurate control of linear and rotational motion of micro/nano-particles on surfaces.
- + The lack of dry particle removal techniques in nanoscale has also been a problem in various areas of nanotechnology (for example, UEV lithography). Below 60nm particle removal with dry techniques appears an open problem.



# MEMS Stiction and Friction Characterization System

Tim Dallas  
Texas Tech University

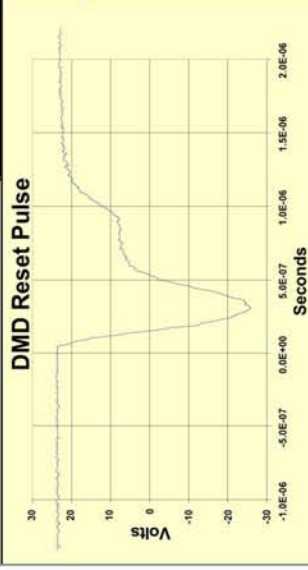
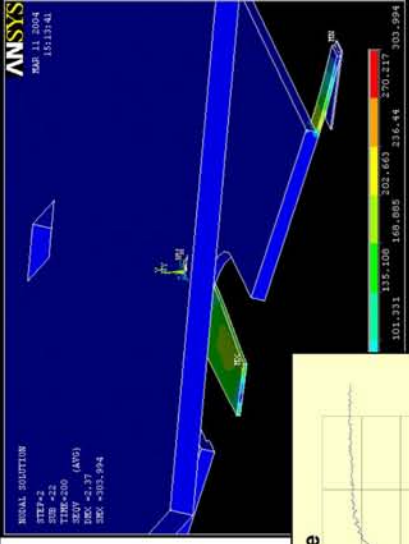
## Goals and Potential Impact if Successful

- Understand stiction and friction in a MEMS as a function of surface chemistry and ambient environment
- Understand stiction caused failure modes
- Reduction in stiction/friction through improved processing and materials
- 3-D computer model of MEMS device including stiction and friction effects
- Extend grad/undergrad education in control and actuation issues in MEMS
- Impact: Non-hermetic packaging of MEMS

## Approach and/or Accomplishments

- Use Texas Instrument's Digital Micromirror Device (DMD) as test system
- Building gas manifold system to vary environmental conditions of packaged atmosphere
- Measuring surface energy variation due to materials and processing issues
- Development of control and detection hardware and software to actuate mirrors and analyze response
- Built custom controllers for varying actuation voltage (DC & AC) and pulse duration
- Building 3-D multi-physics model of a DMD using ANSYS FEM software

## DMD FEM modeling



## DMD control pulse generation

## Bottlenecks and Open Research Questions

- How to quantify surface coverage and mobility of anti-stiction self-assembled monolayers (SAMs)
- Impact of dynamic actuation on SAM adhesion, durability, and mobility
- Very difficult to characterize interaction regions of contacting components in MEMS
- Mechanical properties of sub-micron structures: issues concerning contact area and metal fatigue
- Multidisciplinary problems that combine high speed electronic control with surface chemistry



# Design and Control of Arrayed MEMS

Gary K. Fedder  
Carnegie Mellon University

## Goals and Potential Impact if Successful

MEMS arrayed control has numerous applications: micro/nano manipulation systems, optical beam steering, ciliary actuators, and probe-based data storage, inspection and sensing.

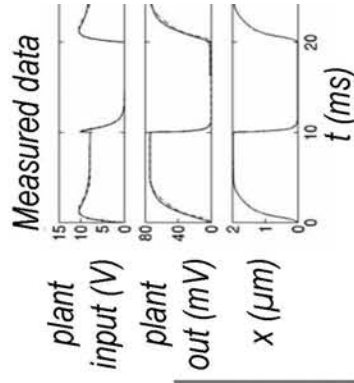
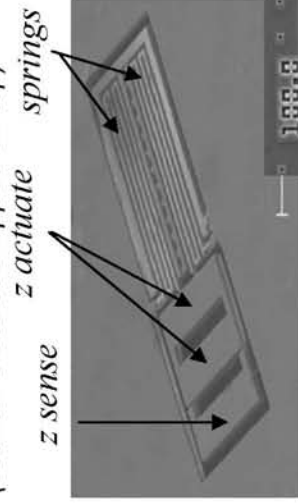
Massively parallel microservo manipulators with nanometer precision will help pave the way to manufacture of micro/nano systems that cannot be made with conventional batch fabrication. Robust interfacing to micro/nano parts requires control systems with local sensing and actuation. Such microservo systems may work synergistically with self-assembly techniques.

## Approach and/or Accomplishments

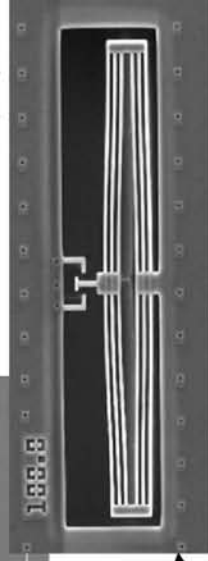
Arrayed control can be achieved through integration of MEMS with electronics. Servo micromechanisms include embedded sensing and actuation for each degree of freedom. These functions can be integrated into compact cells with modular design for tiling in arrays. Complexity is supported with a mixed-physics/electronics design environment.

Key challenge problems must be identified to drive the research. For example, robust gear on peg placement and/or nanotube placement would be appropriate to drive understanding of issues in manipulation at these respective scales.

CMOS-MEMS parallel-plate (p-p) microactuator with capacitive sense (counter electrode flipped on top)



Electrothermal actuator,  
25  $\mu\text{m}$  in x for 40  $\mu\text{m}$  by  
200  $\mu\text{m}$  layout



## Bottlenecks and Open Research Questions

To date, most successful micromechanical systems interact without contact physics, especially contact with things existing off chip. The presence of Van der Waals, surface tension and surface charge forces poses challenges in manipulation. Research is needed at the device and system level to characterize these phenomena under practical circumstances, modeling and verification for various materials encountered in micro/nano systems. Local control methodologies and associated engineering implementations that reject on- and off-chip disturbances and are robust under plant uncertainty must be found. Handling the design complexity of large integrated microsystems remains a challenge as well.



# Integrated Microsystems for Industrial Flow Control

Albert K. Henning  
Redwood Microsystems, Inc.

## Goals and Potential Impact if Successful

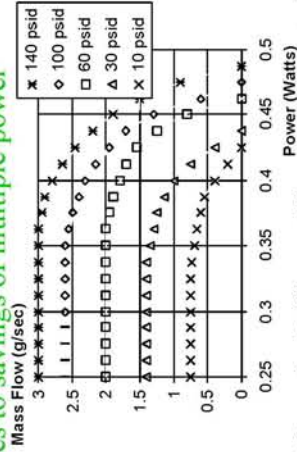
Substantial improvements in yield, throughput, reliability and overall cost of ownership for semiconductor process tools

Reduction in size and cost, and increase in reliability, of industrial pneumatic control systems

3-12% improvement in residential refrigeration energy efficiency through active flow control (translates to savings of multiple power plants per year on a national basis)

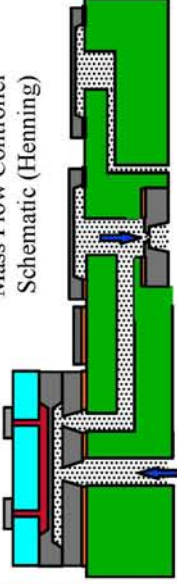
Improvement of automotive fuel injection and emissions controls systems, reducing fuel consumption and waste emissions

Reliability and safety improvements for all manner of industrial flow control systems

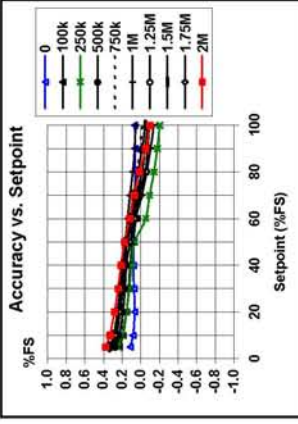
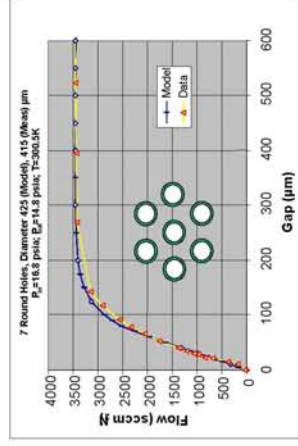


Microvalve Refrigerant Flow (Henning, *et al.*)

Mass Flow Controller Schematic (Henning)



Capacitive Pressure Sensor (Zias, *et al.*)



MFC Reliability (Lawrence & Henning)

Microvalve Flow Model (Henning)

## Accomplishments

Integrated MEMS-based flow control systems for distribution and control of semiconductor process gases, with high performance, accuracy, repeatability, and reliability

Development of integrated flow control systems using silicon MEMS components, compatible with all relevant gases except atomic fluorine

Development of MEMS component packaging techniques with low stress, low drift, and high reliability

Development of compressible gas flow models for SPICE-like, steady-state and transient flow modeling of orifices, microchannels, and microvalves

Development of comprehensive design tools (modeling of actuation and flow) and fabrication technology for microvalves

Development of MEMS-based refrigerant flow control technology

Novel, wide dynamic range pressure sensor

Flow delivery systems for microscale chemical reactors

## Bottlenecks and Open Research Questions

Reliable, corrosion-resistant coatings for silicon and other system materials; materials compatibility between controlled fluid and system materials; mechanical properties of microfabrication materials.

Physics of coefficient of discharge in micrometer-scale orifices as function of pressure, temperature, gas type and shape; effect of departure from assumptions of ideal gas behavior, adiabatic flow, and isentropic flow; effects of fluid interaction with channel walls

Robust tools for transient simulation of compressible gas flow in highly integrated microsystems

Characterization of and calibration between modeling tools (lumped and FEA) and actual hardware

Physics of discrete vs. continuum flow for Knudsen and molecular flow, as system sizes shrink to the micro and nanoscale

Need for fast response, high force, high displacement, low energy/power actuation mechanisms



# Control of flow in Chromatography and Biosensing

Peter J. Hesketh  
Georgia Institute of Technology

## Goals and Potential Impact if Successful

Detection of bio and chemical hazards rapidly in small sample volumes with high selectivity and sensitivity.

Separation of complex mixtures to reduce false positives. Preconcentration to increase sensitivity of measurement.

GC: Fast acting microvalve for sample injection. Multiple analyte separation with different column temperatures, column coatings, and flow rates.

Bioassay: Arrays of parallel assays are necessary to increase statistics and carry out positive and negative controls. Integration of the fluidics with sensors and flow control in aqueous buffer is required. Surface biocompatibility is required and sterilizability may be important for clinical samples.

## Approach and/or Accomplishments

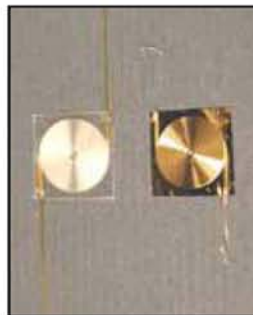
GC: Latching miniature electromagnetic valve demonstrated with actuation current of 0.4A, 2V and a response in under 0.1ms. Operates in air or water/methanol solutions. The pressure drop is <<1kPa at 1 ml/min flow and provide low leakage for 24 hours at 57kPa pressure.

MicroGC with low thermal mass, rapid response, and commercial flame ionization detector demonstrated.

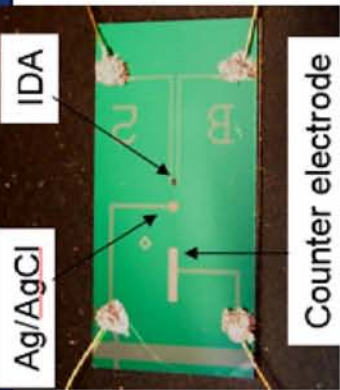
Bioassay: Sandwich assay demonstration with magnetic beads (2.8µm dia.) in a fluid channel. Detection of 70 amole of β-galactosidase (enzyme label on secondary Ab) and 90ng/ml of MS2 bacteriophage.



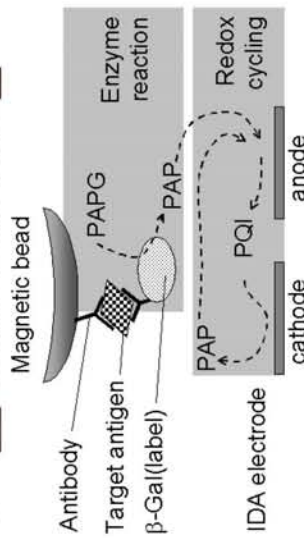
Miniature latching microvalve



1m parylene GC column



Counter electrode



## Bottlenecks and Open Research Questions

1. Pre-concentration of sample.
2. Sample injection with minimal dispersion.
3. Microvalve dynamic characteristics.
4. Uniform coating of the column with different stationary phases, and characterization of coating uniformity.
5. Ultimate sensitivity of assay with magnetic beads.
6. Control of sample volume, fluid flow velocity, magnetic bead location, sample mixing and incubation in a highly parallel format assays.



# Disk Drive Servos for 1 Tera-bit/in<sup>2</sup> Storage Densities

Roberto Horowitz  
University of California at Berkeley

## Goals and Potential Impact if Successful

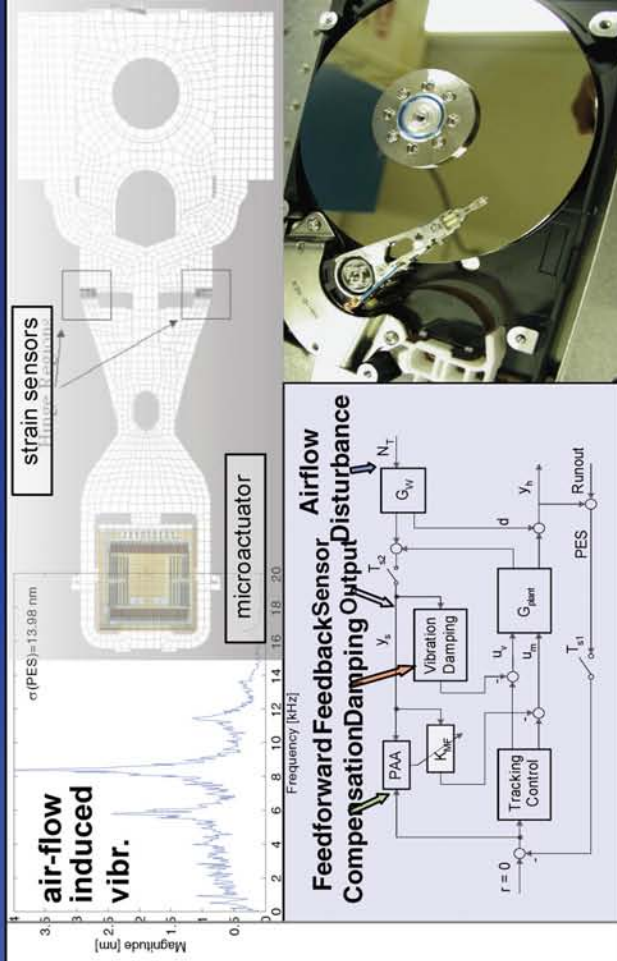
Develop servo technology to attain 1 Tera-bit/in<sup>2</sup> storage densities in magnetic recording disk drives by achieving a track-following positioning error variance of less than 5 nanometers in the presence of:

- **Airflow-induced structural vibrations in the actuator arm, E-block and suspensions (1-20 kHz region).**
- **Non-repetitive disk runout and actuator bearing friction.**
- **Limited sample rate in the position error signal (PES).**
- **A slider flying height of less than 5 nanometers.**

The results of this research could strongly affect the future of the magnetic disk drive industry, which currently has \$20B in annual revenues.

## Approach and/or Accomplishments

- 1) Track-following dual-stage servo systems comprised of:
  - Voice-coil motor for coarse positioning
  - MEMS microactuator for fine/high bandwidth tracking with relative positioning capacitance position sensing.
  - MIMO servo architecture designed using mixed H<sub>2</sub>/H<sub>∞</sub> optimization criteria.
- 2) Vibration suppression and compensation servo systems:
  - Instrumented suspension with embedded vibration strain sensors.
  - Active damping and feedforward compensation control systems.



## Bottlenecks and Open Research Questions

- Develop new fabrication techniques for high performance and structurally robust MEMS microactuators.
- Develop new MEMS fabrication technologies for embedding silicon sensors and microstructures on metal wafers.
- Develop control-oriented design methodologies for determining optimal strain and vibration sensors configurations that maximize sensing of vibration modes that contribute to off-track errors while minimizing sensing of modes that do not contribute to off-track errors.
- Implement MIMO and multi-rate control systems that achieve optimal tracking and vibration suppression, while maintaining robustness to modeling uncertainties.



# Functional/structural integration of microbiosensor using “electrochemical actuation”

Chang-Soo Kim  
University of Missouri-Rolla

## Goals and Potential Impact if successful

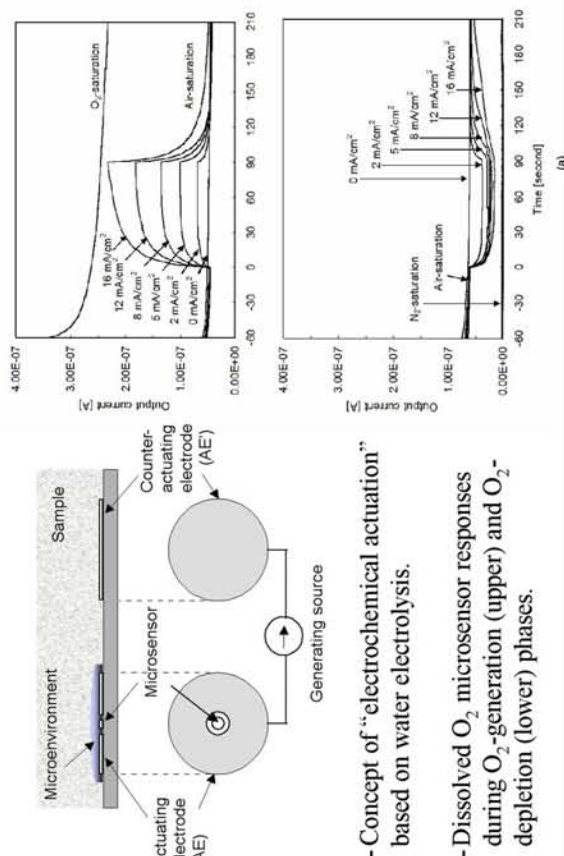
- Advanced control and system integration**; intelligent biochemical sensors in infant stage. achievement of FUNCTIONAL INTEGRATION (built-in intelligence) as well as structural integration (miniaturization).
- Realization of self-calibration/self-diagnosis function for (micro) biochemical sensor**; periodic correction of baseline drift and sensitivity degradation.
- Eventual goal**: implementation of intelligent, self-regulatory and autonomous microbiosystem (automated lab-on-a-chip, continuous biochemical/medical monitoring, closed-loop drug delivery, etc.).

## Approach and/or Accomplishments

- “Electrochemical actuation” based on water electrolysis by using integrated actuation electrode (AE)**; manipulation of microenvironments of oxygen and pH gradients surrounding the microsensors.  

$$2\text{H}_2\text{O} \rightarrow 4\text{H}^+ + 4\text{e}^- + \text{O}_2 \text{ (at AE as anode)}$$

$$2\text{H}_2\text{O} + 2\text{e}^- \rightarrow 2\text{OH}^- + \text{H}_2 \text{ (at AE as cathode)}$$
- Applications**; 2-point self-calibration/self-diagnosis for dissolved oxygen microsensor, 1-point for glucose microsensor, microscale pH titration.
- Microsystem integration**; electrochemical microactuator and microbiosensor in a chip.



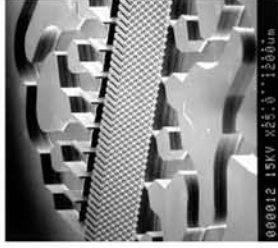
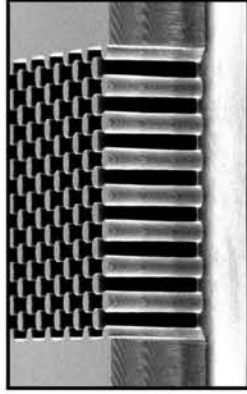
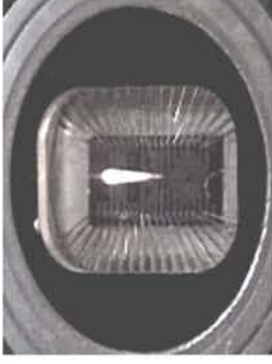
- Concept of “electrochemical actuation” based on water electrolysis.
- Dissolved O<sub>2</sub> microsensor responses during O<sub>2</sub>-generation (upper) and O<sub>2</sub>-depletion (lower) phases.

## Bottlenecks and Open Research Questions

- Main focus of current micro/nanoscale sensor research activity**; mostly on miniaturization and exploratory use of new materials.
- Main obstacle to further R&D and practical utilization**; absence of built-in *in situ* intelligence (self-regulation, self-calibration, autonomy).
- Limitation of exemplary “electrochemical actuation” based on water electrolysis**; applicable to the defined electrolyte solution (model system) only, and limited to oxygen, pH and some enzyme reactions (e.g. oxidase).

## Goals and Potential Impact if Successful

- We are developing micro/nano fluidics for chemical processing and power generation.
- The goal is to aggressively scale and integrate functions
- Chemical processing at the microscale can change the way in which synthesis and analysis in the chemical industry is currently performed
- Biological processed (e.g. fermentation) also can be impacted by this technology wherein parallel processing is enabled
- Power generation at this scale enables battery alternatives in certain applications



## Approach and/or Accomplishments

- Implementation of chemical reactors for gas-gas, gas-liquid, and liquid-liquid reaction.
- Demonstration of fuel reformers and hydrogen purification devices
- Implementation of microscale bioreactors
- Power generation in thermoelectric and thermophotovoltaic microsystems.

## Bottlenecks and Open Research Questions

System integration issues are the dominant bottleneck. The challenges are:

- Packaging
- Chemical compatibility
- Heat management
- Interconnect reliability (both fluidic and electric)
- Components (valves, pumps)
- Control of multiple reactor systems



# Characterization of Micro and Nano Components for Complex Systems

Sharon Smith  
Lockheed Martin Corporation

## Goals and Potential Impact if Successful

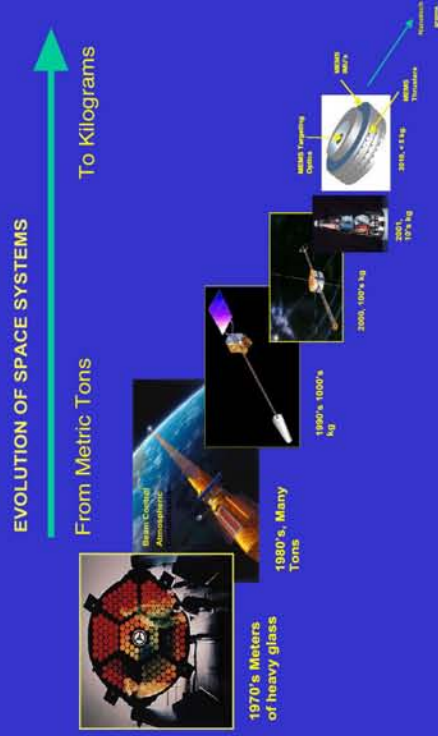
The new materials processing associated with micro and nano components has taken us into the domain of atomic engineering. We need to create and understand the physics associated with atomic scale devices (including MEMS and micro systems which have surface nano properties). Surface and quantum effect become significant over performance and failures dominated by the bulk (classical) effects of the devices or material properties.

## Approach and/or Accomplishments

**Areas of interest** to be addressed include: carbon nanotubes and other “designer” materials (e.g., for a spectrum of sensors), advanced EO polymers, thin film photovoltaics, and adaptive optics

**Approach:** Understand the underlying physics and failure modes with modeling and simulation tools that characterize the atomic and molecular properties, all supported by experiments

## Trend in Space Systems



## Bottlenecks and Open Research Questions

### **Qualification of our technology:**

- To understand the effects that the environment (e.g., radiation effects and extremes in temperature and pressure) and applications have on our end products such as space, missile and aeronautical systems
- With better first principle tools, models, and simulations. We generally lack these first principle tools and so do some of our principle suppliers

## Goals and Potential Impact if Successful

- To Develop Modeling & Simulation Software That Allow High-Fidelity, Ab-initio Design of Integrated Bio-micro and Bio-nano Systems
- These tools, if developed, will
  - Reduce development time and costs
  - Enhance performance through optimization
  - Further innovation by increased understanding and rapid concept screening
  - Consolidates and disseminates knowledge in a way that new community members (students, starting investigators) can be trained rapidly

## Approach and/or Accomplishments

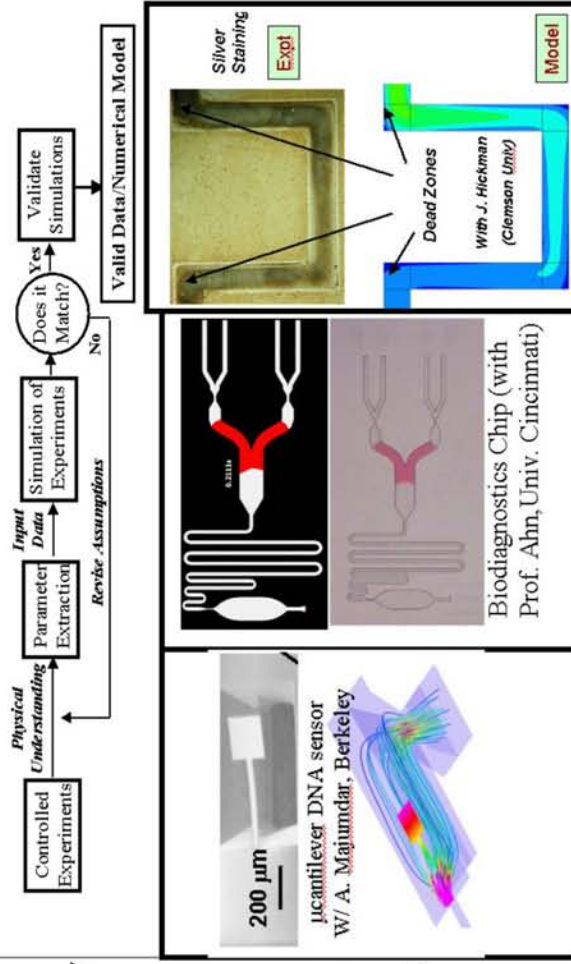
### Modeling

In the past, we have developed a multi-physics S/W environment (CFD-ACE+) that

- is general-purpose (3D, transient) CFD-based
  - solves for fluidic-thermal-biochemical-electrical-magnetic phenomena in a fully coupled fashion
- The physical models have been developed in the context of several BioMEMS investigations

### Experiments

Microfluidics expts to develop and validate models have been carried out at CFDRC and collaborator organizations (U.C. Berkeley, Stanford, Clemson etc.)



## Bottlenecks and Open Research Questions

- Acceptance and consistent usage of microfluidic (non-microarray) platforms in Biotech/Pharma. Lack of standardization
- Prediction methods and/or specialized databases for ab-initio estimation of simulation parameters to enable quantitative modeling
- Consistent, Accurate and Rapid Hierarchical Models for Integrated Nanosystems featuring (this will also enable real-time control modeling efforts)
  - Nanoscale feature models
  - Microscale component models
  - Macroscale system models



# An Integrated Biosensor System for Cellular Studies\*

Marvin White and Santosh Pandey  
Lehigh University, Bethlehem, PA

## Goals and Potential Impact of Research

Our goal is to fabricate a silicon-based biochip for rapid screening of pharmaceutical drugs and their effect on targeted single ion channels. The potential impact of this research is to understand the role ion channels play in various diseases, such as MS, Alzheimer's, cardiac arrhythmias, migraine headaches, glaucoma, cancer, memory disorders, immunosuppressant, and a range of other diseases. Our long range goal is to sequence DNA electronically.

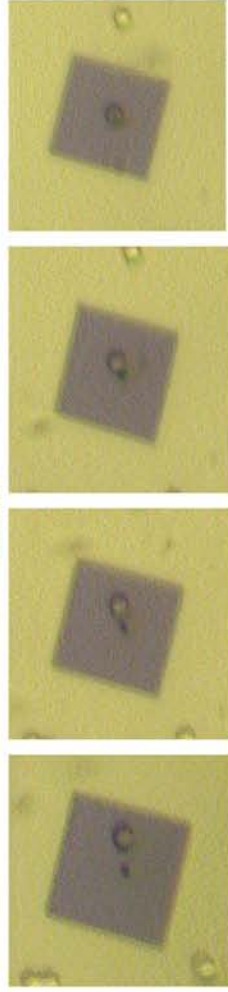
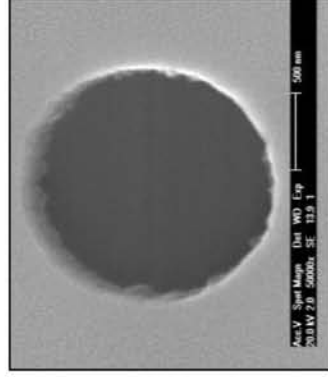
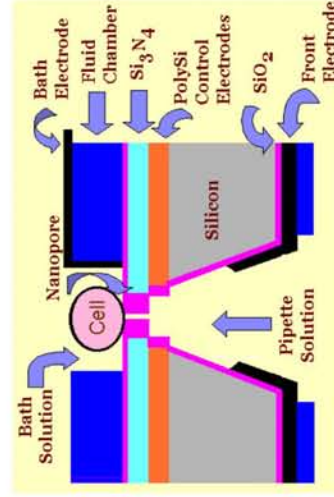
Statistically, 10-20% of the drugs in development today act by affecting voltage-gated ion channels. In addition, 40% of the known human diseases are caused by dysfunctional voltage-gated ion channels.

## Approach and Accomplishments

We have constructed a planar patch-clamp measurement system on a chip with nanopores drilled in a membrane resting on multiwell reservoirs.

We have examined the driving forces needed to manipulate single cell movement in the vicinity of a nanopore with the use of dielectrophoresis.

We have designed, simulated and are constructing an integrated CMOS instrumentation amplifier to process 1-10 pA, 1-2.5 kHz, single ion channel current recordings.



## Bottlenecks and Research Issues

A feedback control system is required to sense the leakage current between the cell and the nanopore, and to lower this current by varying the electric field strength to achieve a so-called 'gigaseal'.

The integration of the MEMS patch-clamp chip with a CMOS instrumentation amplifier and associated electronics.

The gap between the two fields (i.e. integrated electronics and the biosciences) needs to be strengthened in university curricula.

Software development is required to record and analyze short-time, data streams from the integrated silicon-based biochip.

\*Supported by NSF: ECS – 540297 Program Director: Dr. Rajinder P. Khosla

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